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(54) Title: NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF

(57) Abstract

Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.

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NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 α , IL-1 β and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 α and IL-1 β are proinflammatory cytokines which elicit biological responses, whereas IL-1ra is an antagonist of IL-1 α and IL-1 β activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1RtI) and type II IL-1 receptor (IL-1RtII). Recent results suggest that the IL-1RtI is the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

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protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products described above.

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Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor activation by inhibiting the binding of IL-1 α and IL-1 β to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

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deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250,
5 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID
15 NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the
20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID
25 NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide
30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,
35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

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an amino acid sequence encoded by the cDNA of ATCC Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a
5 complement thereof under stringent conditions.

Also within the invention are: an isolated Tango-77 protein having an amino acid sequence that is at least about 45%, preferably 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:5, SEQ
10 ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11 (immature human Tango-77).

Also within the invention are: an isolated Tango-77 protein which is encoded by a nucleic acid
15 molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807; and an isolated Tango-77 protein which is encoded by a nucleic acid molecule having a nucleotide sequence
20 which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding strand of the cDNA of ATCC 98807, or the complement thereof.

25 Also within the invention is a polypeptide which is a naturally occurring allelic variant of a polypeptide that includes the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an
30 amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

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NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect
5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the
10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)
15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the
20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a
25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing
30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at
35 least one biological activity possessed by naturally

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occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to
5 interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10 The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that
15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20 In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that
25 the presence of Tango-77 activity or expression is detected in the biological sample.

In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or
30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

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agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments, the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

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compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

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Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1ra (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

5 Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The
10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including
20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 kDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding
25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms
30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an

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admission that a deposit is required under 35 U.S.C.
§112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain
5 conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or
10 nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a
15 second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or
20 "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined in vivo, or in vitro, according to standard techniques. A Tango-77 activity can be a direct activity, such as an
25 association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following
30 activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

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inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides
5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which
10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells),
15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal
20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes
30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

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cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

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hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other mammals. The probe/primer typically comprises

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substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807. Alternatively, the oligonucleotide can typically comprise a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of Tango-77 protein (e.g., by recombinant expression in

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vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations in

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Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C. Preferably, an isolated nucleic acid molecule

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of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring
5 nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic
10 variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby
15 leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity
20 and thus would likely be targets for alteration. Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-
25 type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino
30 acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention
35 pertains to nucleic acid molecules encoding Tango-77

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proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

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valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-
30 stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or
35 part of the protein coding region (or open reading

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frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence 5'-TGCAACTTTTACAGGAAACAC-3' (SEQ ID NO:19) or 5'-CCTCACTTTTACCCGAGACTC-3' (SEQ ID NO:20) or 5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to

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generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which

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binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-O-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

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ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, Tango-77 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) *Science* 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77 gene in target cells. See generally, Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In preferred embodiments, the nucleic acid molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup et al. (1996) *Bioorganic*

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& Medicinal Chemistry 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

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would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. W0 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. W0 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,

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hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5 One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide
15 can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

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medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

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amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)

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Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990)

5 J. Mol. Biol. 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST

10 program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402.

15 When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for

20 the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a

25 PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating

30 percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77

35 polypeptide. A "Tango-77 polypeptide" refers to a

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polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein, preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., supra). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of

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melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al.,
5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a
10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction
15 between a Tango-77 ligand and a Tango-77 receptor on the surface of a cell, to thereby suppress Tango-77-mediated signal transduction in vivo. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77
20 ligand/Tango-77 interaction may be useful therapeutically for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify
25 Tango-77 ligands and in screening assays to identify molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the
30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as
35 appropriate, alkaline phosphatase treatment to avoid

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undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer

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side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77
5 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by
10 combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a
15 degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be
20 used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use
25 of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura
30 et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate
35 a variegated population of Tango-77 fragments for

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screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with
5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed
10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the
20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors,
25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble
30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave et al. (1993)
35 *Protein Engineering* 6(3):327-331).

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An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The
5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the
10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a
20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces
25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of
30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a
35 biological sample, which naturally contains Tango-77.

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Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')₂ fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally Current

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Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a
5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for
10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, supra; Galfre et al. (1977) *Nature* 266:55052; R.H. Kenneth, in *Monoclonal Antibodies: A New Dimension*
15 *In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) *Yale J. Biol. Med.*, 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the
20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized
25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3-
30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using
35 HAT medium, which kills unfused and unproductively fused

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myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP™ Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art,

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for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; 5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature* 15 321:552-525; Verhoeyan et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice 20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77. 25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic 30 mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion 35 of this technology for producing human antibodies and

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human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, 5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a 10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments. 20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random 25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to 30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to 35 guide the selection of human heavy chain genes as

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follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to
5 phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human
10 antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody. The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is
15 described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or
20 immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular
25 lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for
30 example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials,
35 bioluminescent materials, and radioactive materials.

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Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and
5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example
10 of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to
15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of
20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous
25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon
30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

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DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an in vitro transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression

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vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated in vitro, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia

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Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann et al. (1988) *Gene* 69:301-315) and pET 11d (Studier et al., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 60-89). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 *gn10*-lac fusion promoter mediated by a coexpressed viral RNA polymerase (T7 *gn1*). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 *gn1* gene under the transcriptional control of the lacUV 5 promoter.

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada et al. (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1

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(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (Invitrogen Corp, 5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series 10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a 15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral 20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory 30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular 35 promoters of T cell receptors (Winoto and Baltimore

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(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the α -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

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Weintraub et al. (Reviews - Trends in Genetics, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride coprecipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome.

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In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable
5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably
10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a
15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises
20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or
25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a
fertilized oocyte or an embryonic stem cell into which
30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77
35 sequences have been altered. Such animals are useful for

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studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

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of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e., no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby

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alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to
5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination
10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic
15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal
20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and
25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing
30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

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In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G₀ phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

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IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be
5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the
10 language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use
15 of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal
25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene
30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as
35 acetates, citrates or phosphates and agents for the

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adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable
5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable
10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be
15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing,
20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance
25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid,
30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

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in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a

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glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5 For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10 Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and
15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For
transdermal administration, the active compounds are
20 formulated into ointments, salves, gels, or creams as generally known in the art.

 The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention
25 enemas for rectal delivery.

 In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and
30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to
35 those skilled in the art. The materials can also be

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obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as
5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or
10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active
15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the
20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors.
25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the
30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g.
35 retroviral vectors, the pharmaceutical preparation can

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include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

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antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and
5 uses thereof for treatments as described herein.

A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents
10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular
15 libraries can be found in the art, for example in:
DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909;
Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422;
Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et
al. (1993) *Science* 261:1303; Carrell et al. (1994) *Angew.*
20 *Chem. Int. Ed. Engl.* 33:2059; Carell et al. (1994) *Angew.*
Chem. Int. Ed. Engl. 33:2061; and Gallop et al. (1994) *J.*
Med. Chem. 37:1233.

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-
25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith
30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

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In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the
5 Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a
10 non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the
15 receptor and inhibiting future signal transduction. Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the
20 Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the
25 target (e.g., intracellular Ca^{2+} , diacylglycerol, IP3, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid
30 encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a
Tango-77 protein or biologically active portion thereof
35 with a test compound and determining the ability of the

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test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay comprises contacting the Tango-77 protein or biologically

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active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

10 It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a
15 solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide,
20 Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)_n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-dimethyl-3-ammonio-1-propane sulfonate.
25

In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms
30 of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for
35 containing the reactants. Examples of such vessels

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include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For
5 example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined
10 with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or
15 microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity
20 determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of
25 biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated
30 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77
35 trapped in the wells by antibody conjugation. Methods

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for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as 5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of 10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate 15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, 20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate 25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) *Cell* 72:223-232; Madura et al. (1993) *J. Biol. Chem.* 268:12046-12054; 35 Bartel et al. (1993) *Bio/Techniques* 14:920-924; Iwabuchi

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et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such
5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular
10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known
15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If
20 the "bait" and the "prey" proteins are able to interact, in vivo, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ)
25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes
30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

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B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

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mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, e.g., colcemid that disrupts the mitotic spindle. The

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chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be
5 used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases
10 will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (Human Chromosomes: A Manual of Basic Techniques (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used
15 individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding
20 sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the
25 sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, Mendelian Inheritance in Man, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the
30 same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) *Nature* 325:783-787.

Moreover, differences in the DNA sequences between
35 individuals affected and unaffected with a disease

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associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

2. Tissue Typing

The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

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sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or dead, can be made from extremely small tissue samples.

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3. Use of Partial Tango-77 Sequences in Forensic

Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments. Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

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example, an in situ hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence of a mixture of different types of cells in a culture).

C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.

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Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in clinical trials.

These and other agents are described in further detail in the following sections.

1. Diagnostic Assays

An exemplary method for detecting the presence or absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

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conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of Tango-77 mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of Tango-77 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of Tango-77 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

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labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting Tango-77 protein, mRNA, or genomic DNA, such that the presence of Tango-77 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of Tango-77 protein, mRNA or genomic DNA in the control sample with the presence of Tango-77 protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of Tango-77 in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of Tango-77 (e.g., an immunological disorder). For example, the kit can comprise a labeled compound or agent capable of detecting Tango-77 protein or mRNA in a biological sample and means for determining the amount of Tango-77 in the sample (e.g., an anti-Tango-77 antibody or an oligonucleotide probe which binds to DNA encoding Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:6, or SEQ ID NO:10). Kits may also include instruction for observing that the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77 if the

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amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

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at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant

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inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting
5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene;
10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an
15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77
20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a
25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.,* U.S. Patent Nos. 4,683,195 and
30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.,* Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for
35 detecting point mutations in the Tango-77-gene (*see,*

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e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA

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indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotides probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a

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variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the 30 control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

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"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77 sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in

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electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing
5 a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of
10 approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

15 Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the
20 known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides
25 are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification
30 technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on
35 differential hybridization) (Gibbs et al. (1989) *Nucleic*

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Acids Res. 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) Tibtech 11:238). In addition, it may be desirable to
5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) Mol. Cell Probes 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany
10 (1991) Proc. Natl. Acad. Sci USA 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of
15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used,
20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is
25 expressed may be utilized in the prognostic assays described herein.

3. Pharmacogenomics

Agents, or modulators which have a stimulatory or
30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma)
35 associated with aberrant Tango-77 activity. In

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conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens.

Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

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malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes

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to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

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and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as
5 described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of
10 the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention
15 provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the
20 steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples
25 from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample
30 with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or
35 activity of Tango-77 to higher levels than detected,

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i.e., to increase the effectiveness of the agent.
Alternatively, decreased administration of the agent may
be desirable to decrease expression or activity of
Tango-77 to lower levels than detected, i.e., to decrease
5 the effectiveness of the agent.

C. Methods of Treatment

The present invention provides for both
prophylactic and therapeutic methods of treating a
subject at risk of (or susceptible to) developing or
10 having a disorder associated with aberrant Tango-77
expression or activity. Alternatively, disorders
associated with aberrant IL-1 production can be treated
with Tango-77. Such disorders include acute and chronic
inflammation, asthma, some classes of arthritis,
15 autoimmune diabetes, systemic lupus erythematosus and
inflammatory bowel disease.

1. Prophylactic Methods

In one aspect, the invention provides a method for
preventing in a subject, a disease or condition
20 associated with an aberrant Tango-77 expression or
activity (or aberrant IL-1 expression or activity), by
administering to the subject an agent which modulates
Tango-77 expression or at least one Tango-77 activity.
Subjects at risk for a disease which is caused or
25 contributed to by aberrant Tango-77 expression or
activity can be identified by, for example, any or a
combination of diagnostic or prognostic assays as
described herein. Administration of a prophylactic agent
can occur prior to the manifestation of symptoms
30 characteristic of the Tango-77 aberrancy, such that a
disease or disorder is prevented or, alternatively,
delayed in its progression. Depending on the type of
Tango-77 aberrancy, for example, a Tango-77 agonist or
Tango-77 antagonist agent can be used for treating the

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subject. The appropriate agent can be determined based on screening assays described herein.

2. Therapeutic Methods

Another aspect of the invention pertains to
5 methods of modulating Tango-77 expression or activity for
therapeutic purposes. The modulatory method of the
invention involves contacting a cell with an agent that
modulates one or more of the activities of Tango-77
protein activity associated with the cell. An agent that
10 modulates Tango-77 protein activity can be an agent as
described herein, such as a nucleic acid or a protein, a
naturally-occurring cognate ligand of a Tango-77 protein,
a peptide, a Tango-77 peptidomimetic, or other small
molecule. In one embodiment, the agent stimulates one or
15 more of the biological activities of Tango-77 protein.
Examples of such stimulatory agents include active
Tango-77 protein and a nucleic acid molecule encoding
Tango-77 that has been introduced into the cell. In
another embodiment, the agent inhibits one or more of the
20 biological activities of Tango-77 protein. Examples of
such inhibitory agents include antisense Tango-77 nucleic
acid molecules and anti-Tango-77 antibodies. These
modulatory methods can be performed in vitro (e.g., by
culturing the cell with the agent) or, alternatively, in
25 vivo (e.g., by administering the agent to a subject). As
such, the present invention provides methods of treating
an individual afflicted with a disease or disorder
characterized by aberrant expression or activity of a
Tango-77 protein or nucleic acid molecule. In one
30 embodiment, the method involves administering an agent
(e.g., an agent identified by a screening assay described
herein), or combination of agents that modulates (e.g.,
upregulates or downregulates) Tango-77 expression or
activity. In another embodiment, the method involves

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administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

EXAMPLES

Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 α , IL-1 β and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 α , IL-1 β and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 α and IL-1 β were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 α and IL-1 β was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 α and IL-1 β . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

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segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA
5 libraries for the expression of a Tango-77 message. A cDNA library from TNF- α treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated
10 from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID
15 NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ
20 ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted
25 signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

30 The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino
35 acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

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mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human IL-1ra at the amino acid level.

Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with ³²P-dCTP using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF α -treated bronchoepithelium, TNF α -treated SSC cell line and anti-CD3-treated T cells.

Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

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protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

- 5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115
10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

- Mature Tango-77 has a predicted MW of about 13 kDa
15 and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

Example 4: Preparation of Tango-77 Proteins

- Recombinant Tango-77 can be produced in a variety
20 of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused
25 to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by
30 affinity chromatography on glutathione beads.

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Example 5: Alternatively spliced forms of IL-1ra and
Tango-77

Computer program Procrustes (Gelfand et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93:9061-9066) is an alignment
5 algorithm that predicts the presence of alternatively
spliced exons for a protein of interest in a stretch of
genomic DNA. Using the IL-1ra sequence, Procrustes was
used to search for the presence of additional sequences
that might encode for alternatively spliced forms of IL-
10 1ra in the two overlapping BAC genomic sequences (see
Fig. 3 and Fig. 4). Potential sequences that encode
variant exons for IL-1ra were identified. These
predicted exons aligned well with the N-terminal region
of IL-1ra, but were not present in Tango-77. The results
15 from Procrustes predicts the existence of more spliced
forms of IL-1ra.

Furthermore, Procrustes also predicted an
additional sequence in BAC1 and BAC2 that encodes an
alternatively spliced exon for Tango-77 (T77-procrustes;
20 Fig. 5). This predicted splice variant form of Tango-77,
T77-procrustes, was aligned with Tango-77 (Fig. 6) and
with IL-1ra and IL-1 β (Fig.7).

PCR primers within this sequence can be used to
generate a product that can be used to screen a panel of
25 cDNA libraries using standard techniques. Suitable cDNA
libraries include libraries made from TNF α -treated
bronchoepithelium, TNF α -treated SSC cell line and anti-
CD3-treated T cells. The resulting cDNA clone(s) can be
isolated from the library and sequenced to identify
30 additional Tango-77 cDNAs.

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Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific
5 embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:
 - a) a nucleic acid molecule comprising a
5 nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
20 plasmid deposited with ATCC as Accession Number 98807;
 - d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID
25 NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid
30 deposited with ATCC as Accession Number 98807; and
 - e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

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SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid
5 molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and

15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
20 plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous
25 polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

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7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID
30 NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

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10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID
10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID
15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids
20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
30 plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10
under stringent conditions;

comprising culturing the host cell of claim 5
under conditions in which the nucleic acid molecule is
5 expressed.

13. A method for detecting the presence of a
polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which
selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the
polypeptide in the sample.

14. The method of claim 13, wherein the compound
which binds to the polypeptide is an antibody.

15. A kit comprising a compound which selectively
15 binds to a polypeptide of claim 8 and instructions for
use.

16. A method for detecting the presence of a
nucleic acid molecule of claim 1 in a sample, comprising
the steps of:

- 20 a) contacting the sample with a nucleic acid
probe or primer which selectively hybridizes to the
nucleic acid molecule; and
- b) determining whether the nucleic acid probe or
primer binds to a nucleic acid molecule in the sample.

25 17. The method of claim 16, wherein the sample
comprises mRNA molecules and is contacted with a nucleic
acid probe.

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18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which
5 binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for
20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a
25 sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a
5 test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

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GTGGACCCACGGCTCCGCGACAGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGCCCAGGGGAAACTTA 79
GGCAGGGCGAGCGGACGGGCACCTCCCGCGGGACGAACTCACTCGGTGGCCTCCTACTTCCCGGGCCGTGTTCCAACGCC 158
TGAGAATAACGGGAACAGCGGTCTGTACTCACCGACAGCGGCAGCAGCGGCCTCTCTCAATTGGGCAAAGCACTCCAGAC 237
CTTTTGGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCTCAGCTTCTACGCAAGTATAAGTCTTGGACTT 316
      M   S   F   V   G   E   N   S   G   V   10
CATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAA ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 185
      K   M   G   S   E   D   W   E   K   D   E   P   Q   C   C   L   E   D   P   A   30
AAA ATG GGC TGT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445
      G   S   P   L   E   P   G   P   S   L   P   T   M   N   F   V   H   T   K   I   50
GGA AGC CCC CTG GAA CCA GGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505
      F   F   A   L   A   S   S   L   S   S   A   S   A   E   K   G   S   P   I   L   70
TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565
      L   S   V   S   K   G   E   F   C   L   Y   C   D   K   D   K   G   Q   S   H   90
CTG GGG GTC TCT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625
      P   S   L   Q   L   K   K   E   K   L   M   K   L   A   A   Q   K   E   S   A   110
TCA TCC CTT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685
      R   R   P   F   I   F   Y   R   A   Q   V   G   S   W   N   M   L   E   S   A   130
CGC CGG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745
      A   H   P   G   W   F   I   C   T   S   C   N   C   N   E   P   V   G   V   T   150
GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805
      D   K   F   E   N   R   K   H   I   E   F   S   F   Q   P   V   C   K   A   E   170
GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865
      M   S   P   S   E   V   S   D   *   179
ATG AGC CCC AGT GAG GTC AGC GAT TAG 892
GAAACTGCCCCATTGAACGCCCTTCTCGCTAATTTGAACTAATTGTATAAAAAACACCAAACCTGCTCACTAAAAA 971
AAAAAAAAGGGCGGCCGC 989

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Fig. 1

1 50
 IL1ra-human MEICRGLRSH LITLLFLFH SETICRPSGR KSSKMQAFRI WDVNQKTFYL
 T77-human -----
 IL1b-human -----
 Consensus -----
 51 100
 IL1ra-human RNNQLVAGYL QGPNVNLEEK IDVVPIEPH. ALFLGIHGGK MCLSCVKSGD
 T77-human -----
 IL1b-human -----
 Consensus -----
 101 150
 IL1ra-human ETR..LQLEA VNITDLSNR KQDKR.FAFI RSDSGPTTSF ESAACPGWFL
 T77-human QSHPSLQLKK EKLMKLAQK ESARRPFIFY RAQVGSWNML ESAAHPEWFI
 IL1b-human K..FTLQLES VDPKNYP..K KRMEKRFVFN KIEINNKFES ESAQFPNWI
 Consensus -----
 151 192
 IL1ra-human CTAMEADQPV SLTNMPDEGV MVTKFYFQED E-----
 T77-human CTSCNCNEPV GVTDKFENRK HI.EFSFPV CKAE MSPSEV SD
 IL1b-human STSQAENMPV FLGGT.KGGQ DITDFTMQFV SS-----
 Consensus -T-----PV -----F--Q--

FIG. 2

>Contig1

GAAGTGAAGATATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA
AGGAAATAGAATATATTGGGGAGTAATTATGGGTGTAAAGAAATATAGTA
GGGAAGTATTTAGATTTGAGAAAAAAGGAATTTAGTGTAGGTGAA
NAATAAAAGNANAAGGTTAAAAATTTAAAAAATTAATAATAAATAAAT
AAATAAAAAATAAAATAAAATAAAATTTAAAAAATTAATAATAAATAA
AAAAATAAGAAATGGAAGTGGATTCTTAGAAAAAAGAAAGTAAGGTGA
TAGGAGGATAGAGAGGATGTGGTGTGAGATGATTGGTTTAATTAGAAA
ATAGGTTTTGAATAGAGTGGGAAAGTAGAGTTTGGTAAATGTGGGGGGA
AGAGGGTAATGTTGTTTGAAGTGAAGAAAAAATGGTATATTTTATAAAA
TAATGAGGAAAGTGTGTGAAAAAATTTATTTGGGATTGGGAAGGTGAT
ATATAAGTTGTGGAAAAATTTGGGGGGTGGGGTTTATTTAGGATTAAAA
GTTATTTAAAGAAATGAAAAATGAAATTTTGTGTAATTTGGGGATAAGAA
ATTAATGTTTAGAAAGAAAGGGAAAAAATGAAGAAAAAATTTAGATTT
TGGAAATTTAAAAATTTGTGGGTGTAATAGGAAGGATTTTAAAGGTA
ATTGTGAAGGATTTGTGTGAAAAATAAGGGAGAAAAAATGGGG

>Contig2

GCATCTAACTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA
AACAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG
AAGGAAAAGGCCAAACACTGTGTTAAAAATTTATCCAAATGTGAGGAAAA
GGCAAAGAGAGTAGGTGTGCTTTTAGTGTCTAAGCTGCCTGCCCAAGG
GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTTTTGTAAAAGA
TCAGATAGTAAATCTTTTCAGCGTGAAGAGCATGAGGTCTCTGTCAAAA
TACTCAACCACCATTAACATGAAAGCAGCCAACAGACAACACATGACA
AATGAGTGTGGCTGTGTTCCAGTAAATCTTGATTACAAAAACAGGCAAGA
GGCCAGAGCTGACCCATGGGCCATAGTTTGCTGACCCCTTCTGTAAAGGA
AAGTATTTTGTGTTGACTTGCTGTTTACCATTGATTGAACACAAGGCTCT
GTAAAGTTACTTGTAACTTGCAGAGATTGATGAGTGGCAAGTAATTTT
TATTCACCAGAAATAAAAATTTCTGTTCAGTAGAAAAAGATAAACCAA
CTGTGATATTATGGTCCTG

>Contig3

GGGGTGTCTGTCTACCATGTGCTCGCAGTTCTGTAATAAATGTTCTCTCA
AGATCCTTAAATCTCTTGGAAATTATAAAAATATTGAAAGAGAAGAAC
AGTTTTTAAATATATATATATATATTTTTTTTGGAGATGGAGTCTT
GCTCTGCTGCTCAGGCTGGAGTGCAGTGGCGCAAACCTTGGTTCAACCAA
CCTCTGCCCTCCGGGTTCAAGCGATTCTTCTGCCTCAGCCTCCTGAGTAG
CTGGGACTACAGGCGCCGCCACCACGCCAGCTAATTTTTGTATTTTTA
GTAGAGCAGAGTTTTACTATGTTGGCTAGGCTGGTCTCAAACCTCTGAC
CTTGTTGATCTGCCCCCTTGGCCTCCCAAAGTGTGGGATTACAGGTGTG
AGCCACTGCACCTGGCCAGTTTTTTAAATATATTTTTTAAACACTTGAA
TAAGAGTCAGTGTAACCTAGAAAGTTTAAAAATGCTTCACAGAACACCCAG
GGTTTACATTACAAGATTCTCACAACAAACCTATTGTAAAGGTGAGTAAG
GCATGTTATTACAGAGAAAAGTTTGGGAGCAAACCTGTAAAAAATTATAT
TTTTGTTGATTTTTCTAAGAGAAAGAGTATTGTTATGTTCTCTAACCTC
TGTGATTACTACTTTAAGTGATTTCTTGAGAGCACATGATGATCC

>Contig4

GCCGTTTCATAGAAAACCTGAAAGCAATAAGATGACTAGGTAAGCATGACAT
TTAAAAGGTATTATGGGACGTGGTTACAAAACCAACTCACAACATAAAAA
GTCTTAGGACCTCTCGCTGACTTAGGAGCCTGATCCCAACTCTGAGAATG
ACTCAGTGTGTTACCCTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGA
GTCACCTAGCCAAACAGCCCATATCAAGTACTTGAAACTTTGACTCAGAAAC
CTCAGTGTGAGAACCTTTGACCTAGGAACCACTGTAGTGGTTAACTGCA
ATTTGCACCCCTTAGTTTCAAGGCTTTACAAACCCGGGGGGGGGAGGGGA
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TTACCTTGTAATCCAATTTGAAATGTGTAATTGACATTAGACTTCTATT
TGAATTTGAAATGTCTAAACCAATGTGGTTAAGTTTGTAAAGGTGTGTG
AATTTTGAAGTCTGTACTACATTTTTTTTAAATTTCTTTTTTTTGG
AGTTTTAGGGATTGCTTAGATGGCTAGAAAGATTTTATTCATCAGATTTT

FIG. 3 (1 of 52)

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TAAGTCTGCCTTGGCAGGCACCTTGCAGAGTTTGAAAGAATCAGATATATC
AAATTTGTAGTTTAAATATTTAAGGGAACCTCAATTAACATGCTAGAAA
AGAGAATTAAGTATTTAGGAGGATTTAATATGGTGTGAAAGTTGTGAAAA
TCAAAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAACCAAGG
AAAGGCATGAAGATAGAGTTCTCACACTTGTATCCCTGATCATGAAAAAG
ATCTGC

>Contig5

GGGTTTTTCCGCGTTTTTACCCGAAATCTTCAAGGGATGGGAAAAAGAAA
ATTGCTAAAAAATCTCGGTTTTTGGTTTTTAACAGATATTTACACNTGG
ATCCCATTTATTATGTTGTCCCAAGGTTTTTGGTGGGTTCCCAATCAGT
TAGCCCCCTCCACAGTGAAAGCACTTTACTTTATCACCTTCACCTAAAG
CATAAAATCCAGCTCTTGAAAGCTGCTCCTTGTTAACTGAATATATCCAC
ATCCCAAAAGTAATGATCCATGCTTCATAATCTGCCACGGATGGATGGAT
GGATGGATGGATGGATGGATGGATGAATGGATGGATTGATTCTTG
GAGGATTTGTTGAATTTGGGAAATTCACGCCAGGACAGCTGGCCCCAAC
TGCCCGCGACAATCTGCTCGGTACAAGGGGAGGGTCTGGAGAGGGTGCG
GCCCGAGCCCCAGTTTGGAATGCCAATTTGGCTCTGCAGCCGGCCTTA
GCCACTTGGGTCTGGCGTCCCTCATTATTAGCGCCATGCCGGCTCGGG
TGCTGCCAAGTCCCTGAGAGCAAGCC

>Contig6

CGCGCTCAAGAAAAGCTGAAGTGTGAATGTTCTGTCTACCTTCACAGTAA
ATGCTAAGAGAATGACCCAAGAGCAGAGGGTATCACTCTGCTACGGAGGA
TTGATTGTAAGTGGCTCTCCTGCCTTAGCAAGAAATGCCAGAACCATGGT
CATTCAAGTTCTTGACCAAAACTGCCTTCATGAGAATCAACTTCCCCAA
GAAAAAAAAGCAGAAACAGGCAAGCTTCCAGCATGGTAGGTAATACTG
ACCCCTTCTTCCCTCCTTCTTTGGAGATTCACACAGTAATAATGCATAAA
GCTTTGCCAATGGACTAAGCACTGCCAGGGGTTTTTGTCTGCCTGGAC
TGAAATGCTCTTTTTGCGTTATCATAGAATCCAGTGCAGTCTGAGTAGA
CTCTAAGCAAAAGGGACATTTTTCAAAAAGGCTTTAAATTGCTAGTACAA
AGAAGGCAACAAACTTGCGTAACTGTGGACAGATTAACCTCACTTGGTGT
TTTGGCTCTTCAGTTTTCCCTTGGCTGCCAAGTACTCCTGAAGCTTTCTC
TGCGGCTCTTCTGCAAGCAGGCAAGCAAAAAACGACTGAACCTTTATTT
CGAGAT

>Contig7

GAAGAGCCGCTAACTTGCTGTAGTGATAAGGAATGAACCTAAGGCTAGGGA
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CCTGCTCCTTCCATATGGTTCGGTCTCAGGCTCACTACCGATCAATGGCG
TACTAAAAGCACTAATAGACTCCAACACGTCTGTCTGTGTTTACG
ACAAGCCGTGGAGTTAATCCCTCTGACAGTAGCTCAGATAAGGATGGCT
ATCATGGGCCCCGGAACCTGGGGCATGACGCTCGTCACCAACGCATGAGCTC
CCCAAGTATGCTATACCTGTCCCTATGAAGGGCTTCCAACCTCTATGTGCA
GTCCCCATGTGGAGAGTCAGGTATTGATTGATCAAGCCAGGGGTGTGGTG
AATGGGGAGCTTCTACAGGGGTAATGATAATTGAAATGCACGGTGATGG
GGATTTTCATATTGGTCTCCTAAGGAGATAACAGATTGGATGCGGGGTG
ATATTCCACTGCCAGGGTGTGTACCGAGGGTATCTGCAGGTGGATCTCC
TCCCCACGTTTGATTAATACTCCTGTCTTGGGAAGCATAGACGGGCGGG
GAAATGATGAAGGGTGACCACTCCCC

>Contig8

GGGAACGCAGTGCTCTGTACGATGGCCTTGATTGCGAATTCCTGCAGGGG
GGG

>Contig9

GGCAAGAGATTTAATATTCATTCCATCTTCATTTGGAAGATGAAAAATTG
GGGACCAGAGAGGGGAGGGGACTGGGCCAAGTTTTCAAAGAAAAGTCAGT
AGGAATTGTGAATTCCTGGGGGCCGGGGCCATTAGTGCTGTTTTGGATC
AGTAAATGGAGATGTGAGTTTCAACAGTAACAGGGACATTTTAAATTA
AATGATTTAACCTTTAGAAAAATGTCCTATTTTGTAAATGATGGATTCA
CAGGAAGGTACAAAGAAATGTCCAGAGAGTTCTNTGAGCCCCCTTCAGCCA
GCTTCTTCCAATGTTAACATCTTGCAATTATTATAGTACAACATCAAACT
GGGAAATCGATATTGGTACTGTCCAGATAGCTTACTCAGATTTTGCCAGT
TATACTTCCACTCATTTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT

FIG. 3 (2 of 52)

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TGTGTGTAGCTCTATGCAATTTTATG1...GTAGCTTCATGTAACCAACCA
AATCACAATACTTAACTATGCCCTCATCACAAGACTCTCTCTTGCTATGC
TTTACAGCTGTATCCTCTTCATCTCCAAACCCTAAGCCCACTCACCAGCC
TCCACCATCTCTAATCCCTGGCAACCCTATTCTGTGCTCCATCTCTGT
ATTAATTGTGTTAATTAATGTTATACAAATGGAATCATGAAGTATGTGTC
CTTTGAGATTGGGCTGTTAATTTTTCACTCAGCACAATTTCCGTGAGTCT
AATCCAACCTGTGTGTAGCAGTAATTTCTTCTTATTATTGCTGAATAAT
ATGCCATGGTATGGATGTATCACAGTGTGTCTAATCCTTTGCCCATTTGAA
AGGAATTTGGATAAATTTCCAGGTTTGGCTATTATGAATAAAGTGAACAT
AAGACATGTGTGTACAAATTTGGTGTGATCAAAAGTCTCATTCTCTGG
GATAAATGCCCGGTAATGAAATGGCTGGGTTGTGTGGG

>Contig10

GCAAGAACACAGGCGCGTATTATAACCTTACTACCAAGACCTGAACCCAT
ATAAAGGTTTATGCGTAACAATCATCATCCCTGTTCCAGAAGATTACAGG
TACGACCACGCTGGCTCACCAGCTCAGGTGGGCCAGTACCAGAAATTCT
CCCAACCAACAGTCTGTCTGAAAACAATCGCGGTGACCTCCACGGTTA
GAAAAGCCTGTTTTCAAGTCTGGAATTGCCACATATTAGCTGGGTAAT
TTGGGCATCACATTTACTCTCTCCGAATTTGAGATTGCAAAAACCTCATTG
GATTGTTTTGTGGATTGAAAGAAATAATGTAAATTTAGGCCGAGTGCTTT
GACTTACGCTGTAAATCCTATCACTTTGGGAGGCCAAAGCAGGAGGGTCA
CTTGAGCTCAGGAATTTGAGACCACCTCTGGCAACATAGTGAGATCCTGT
CTCTACAAAAAATTTTTTAAATTTATCCAGCATGGTGGTACACGCTGT
ATTCCAGCTACTCAGGAGCTGAGGTGTGAGGATTGCTAGAACCCTGGGA
SATCAAGTCAACAGTGAGCCGTGGTTGTGCCACTGCCCTCCAACCTCAGT
GACAGAGGAAGACCCTGTCTCAAAAAAAAAAAAAAAAAAGTAGTAAGTTTAA
AGAACTTAGTGAGGCTGGCATATAAATGATATTGTTGATGTTGATGTT
AGCTTGAAGGCACATTTATAGGAGTAGGGATTTTATAACATTATGAGCCT
GAGAGCACATATAATGTTCCC

>Contig11

GGTCTAACATGCTCCAACCTGAAGAAACCCACACTTGTCCGGCAAGGAAA
CTACTACAGATTTCTGACCTACTGTGCAATTCGGGGCATGCGACGGGAC
TGTGTTTCTGGGTACGCTGTCTCAGGTTCTGTGGGATGTAAGAATTCAA
CTTCAGTAGTTCTCTCATAGACGCGGACGAGAGGGGCGTCTTTTTCTCT
GATGAATCTGCCAGATCTTCCACTTCATAGAGTCTAAATCCTCCGATTCTG
ATCTACTGGAGACCCACGTTACAAAACGCTCTAACGTCGGTGACAGCT
CCCCACATAGGGAAAGATCACCTGAGTCTCACTACCTCACATTAGTGCTA
TCTCCAGCCCCATGCTATCTACGAGATGGTCACGCGAGGTTTAAAGGGGTC
TCCGATTCCGGTGGTCCGATTGAGCTAATCGTGGCCCTACGTGAACGATC
ACTCTGCTCGTAACATCGATACAGGGTCGCGCTGACAAATGGTACTACG
TAGGTTCTCAGGTCAATGCCGCGTCACGAATGAGCCTAACTACCCATAA
GTGCACGTACTGTGTACCTTTCTGTTCCGGCAAACCTGCTACTGTATG
CTGTGCTTGTTT

>Contig12

AGGCTCCATGTGCTCTAGCCTGATTATCTTTTTCAAGTGTTTTATTGCTA
ATCTATAAGGCCCTTTTCGTAAATGTTCACTCATTCTTAATTAGATAT
TTTTTTAATGTTGAGTTTTGAGAGTTCTTTAGATATTTTAGATACAAGT
CCATTGTCAAATATGTGATTTACAAATATTTCTCTCAATCTGTAATTTA
GTTTTATCCTCTTAACAGGGTCTTTTGGAGAGCAAATAATTTGATTTTC
ATAAGGTTCAAATTATTAATTTTTCTTGATAGTTCACTTCTAGTGT
TAAGTCTAAAAACTGTGCCTTGTATAGGTACCAAGGTTTCTCCAGTT
TTTTTTCTAGAAGTTTAGAGTTTATGTTTTACATTGGAGTCCATGATCC
ATTGTTAATTAATTTTTGTATATAGGTAGATGTTTAGGTTTAGGGTTTTT
TAAAAAAAATTACATATGTTAATTGCTCCAGTTCCCTTTTATTGAAA
AGGGTATCCTTCCCTCATTGAATTGCCTTTGTGAGAAATTAATTGGACAT
ATTGTGTGAGTCTATTTCTGGGCTCTTTATCATGTTACTTTAAAAAAT
GCATCAGTTCCCTCCACCAATACCTCATTGTCTTGATTATTGCAGTTATAT
AGTAAGCCTTAGCATTAGGAAAAGTGTTTTCTGCTTTATTCTTTNTCA
AAAAATTTTTGGATATTCTAGGGCCTTTACATATAAATTTAAAAATACT
TTGCTATGTCTAACCGAAAGCCTTATGAAGATTTTGATAAGAATTGCAT
TATGCCATATACATTAATTTAAAAAGAACTGATGTCTTTATTAGTTGATT

FIG. 3 (3 of 52)

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CTGCTAATCTATGAACA1AGCATCTCT...CAAAGCATTTAGTCTTTCTT.
AATTTCTGTCATTAATTTTTTAAATTTTCATCCTAAAGATTCTGTATAT
GTTTTGTTGAATTTATGCTTAAGCATTTCACTTTCTTGGTAACAATTATA
AATGATTTTGTGTTTTTATTCCACTAGTTCATTTTCAGTGTGTAGAAAA
GCAATGAAATTTTGTGTGTTGATCTTTGTTCTACATCTTGCAACATTAT
TGAACCTCATTATTAGTTCTAGGAGGTTTTTTCATTTTTCTGTAGATAC
CTTGAGATTTTCTATATAGACAGTCATGTTGTCTGCAACAGGCACAGTT
TTATTTCTTCTTTTCAATCTATATGCCTTTTTTTTTTTTTTGCCTTAT
TGCAGTGGCTAGAACCTCTAGCACTATGTCAAATAGCATTGGTGAAAGCA
GACATCCTTGTTCTTGTCTTAGAGGAACATTTGGTCTTTAATCTTGAT
TGCG

>Contig13

GCGCCTCCTTTCTCTTCCAAAATTTCTCTTGTCTAGTTATTTGTCCAGG
GAAATTTGAAAGCTCACTTACTGTGCAAGTCAGCAGGAAACAACCTGGGTC
TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT
GAGGTAGATTTCTACAAGAACCTTACCTTCTAAGCAGCACTGGGGTTCAT
CTTTTTCCAGTCTCTCAGAGCCCATTTTCACTCCTGAGTTCTCCCCACA
AAGGACATTTTCAACGTTGAGTTTATTACTCAACAGAAAAATGGAATGAAG
TCCAAGACCTAAGGAGATAGAAAGGGGACCAGTTATGGCATCTTCTCACC
CCAGGACACCTTGCTGCATGTCTCTAGTGCTGAACAGACCACTGGCCTTG
CTCTGTAGTTTGAAATGCTCGCTGCAACCAGAAAGGCACCAAGGGGCCAG
ACCATGCTCTCCTGTCTATCACGCCTTCAAAGCAGAAATTTCCCAAACCTT
GAGTCACAGTGCTAACACACGGGGTGCCTAACATTTTGTGATTTTGG
CATTTTACAAAAATAAAAAAGTTAAAAATGCATTGCTCTATTCTT
GGGGCTGGCACACTATTGCCTTTGGCCAAATCCGGTCCCTGACTGTTTTT
TTAAATAAAGTTTATTGAAACACAACCATGCTCTTGTGTACATATTGTC
TCTTGGCTGCTTCGAAGCTACAATA

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GTGTTGCTTTTTTAACACTTACCTAAAATTACTCTGTAATCCATGGATCC
TTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTTCTCCCA
TCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCCAA
CTTACATGCTTTTAAATGTCATATATGTTAATACCGTATACTTTTAAACT
TTCTAAAATAGCATTATTTTATAGCATGAGTGTTCAATTACATTTTGCAT
TATATTTAGAATTTTCTTGTCTCTTCGTTTCTTCTTCTATTATGACTCC
CCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTGAACCTGCAC
TATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAACTA
AGTAAAATTGAGTAATATTAAAACTCAGTTCTTCTCATCTCACTAGCCAC
ATTTCAAGTGCTCAGCAGCCACGTGCGACTAATGACTACTGTACATCAA
CATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTTCATC
CAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTCAT
GGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTATTT
CTGCNACCATTTACCGGGAGAGGCTGGAAATCATCACCAGGCCAACTC
AAAATTATTACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTCTA
CGTGAAGTGTCATTACCTGAAGACGTTAGTGATTAACTTCTTTAAT
CTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCTGGAGCCTCAGTAAA
TTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCTTG
TCCCCTGCTAAATCATGGAGGTTTGGGGATTCTTTAGAGCACCAATAAA
CTTGTTTGTGGAGGCCTGGGGGTTTTCTTCTGACCACAAATAAACTTGTT
TAATCCTAAATGGGTCTGTTAAGAATTCCTTCTTTATTTTGTATATTT
TAAGGCCACAGAAAGGCCTGGGCAAACTCTTGATGGGCTTTTGTATCAT
TCCAGCCTTTGTATAAGAACAAGTGGTTTTTAAATTTTAACTTAACCATTT
AGTCAGTACTGAAACAGTTGTTATAGAGATCTGCATTAGTGAGACCTGGC
CTGCCACATTTCTTTTCTGAAGATCTTATGGTAGTGATCACCTTTGTGA
AAGGAAAATAAATCTTGGGACCTCAAAATCACTAAGCCAAAGAAAAAAGT
CAAGCTGGGAAGAATCTGACACTTAAATCCAACACTGCTAACTCATTCAT
CTCACTCATTCACTTATTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTT
TTTTTTGAAACGAAGTCTTGTCTGTGTCACCAAGCTGGAGTGCAAGTGGAT
CTCAGGTCACTGCAACCTCCACCTCCCGGGTTCAAGCGATTCTCTACCT
CAGACTCCTGAGTAGCTGGAATTACAGGCACCTGCCACCACGCTGGCTA
ATTTTTATATTTTAGTAGAGACGGGTTTACCATGTTTCATCAGGCTGG

FIG. 3 (4 of 52)

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FIG. 3 (5 of 52)

ATTCAACATCATGCTGAA.CCTTTCAA.LATCATCTTGTTTTTAGTAATC
TCCTACCTTAACTCTCTGTCTCTGCTAGTATGGGAAAGATGACCTGAAA
ATCTAACCATTTATTTTTCCCCCATTAAATATCATTATGATTATTGAGA
AGTTAAATAATTGTCTGCTGCTCCTCCAAAAAGACTGAATCAACTAGCAA
CAATAAGAAATTTCTCACAGCTCTGCCAGCATTTTAAAAGAATAGCTTT
ATTGAGCCCAGGAGGTCAAGGCTGCAGTGAGCTGTGATTACACCACTCTA
CCCCAGCCTGGGTGACAGAGCAAAACCTGTCTCAAAAAAGAAATTTAAG
GAACAGCTTTTATTGTTGTAATAATAGACATACAATAAACAGAGCACATATT
TAAATTGTGCACTTATACTTTGATATAACCCTGTGAAAACATCACCACA
ATCAAGATAGTGAATATATTTATCACCTCCTGATACAGTTTAGCTCTGTG
TCCCCACCTAAGTCTCATGTTGAATTGTAATCCCCAATGCTGGGGGAGGG
GCTTTGTGGGAGGTGATTGAATTGTGGGGGTGCACTTCCCCCTGTCTGTT
CTTGAGATAGTGAATGAGCTCTCATGAGCTCCCCCTCACTCACTCTCTTT
CCTGCTGCCATGTGAGGATGTGCTTGCCTCTTCTTTGCCCTTCTGCCATG
ATGTGTTTCTGAGTCTCCTAACCATGCCTCCTGTACAGCTTGCAGAA
CTGTGAGTCAGTTAAATCTCTTTCTTCATAAATTACCCAGTCTCAGGTG
GCTCTTTATAGCAGTGTGAAAAGGAACTAATATACCTCCTAAGTTACCTC
AAGCTTGTTTTTAATTCCTTCTCCTCCCTTCCTTCATTGCCAAGCAAACA
ACCACCTGTTTTCTGTCACTATAGATTAGTTTACATTTTGTGGGTTTTTT
TTTTTTTTGAGACAAGGTCTGACTCTGTTGCACAGGAGCAGAGCAGCGTA
TC

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CGCGTTATAGGAGATGCGAACCTTAAGAAATGATGATAAGGAGACTTTATT
AAATATAATTTGAATTATTTTGCCATTACAGAAATTCTAATTATTTAAA
ATTCTATTACATAATTTTAACTACTGTACTTCCCAAGCTTAGCTTAGAAT
CCTTCTGTGCTGAGGATTAATTTTAAATTTGTCTTTTATAGGCCTTATCTA
AAATCCAAGAATAATTGCCAGAATCAACCACCTTCTAAATCTGTAAGTAG
AAATTAGTCTTTTTAAAAATATGCATTACATAAGTATGATTAGTAATAAAA
ATAATAAAGATGTTAGCAACCTAAAGAACATGATTTGAAAGGTATTTCT
TACAGATATAAAAAACAGTTTGGTTTAAATAAGAGACAATCATTTTTTGA
AGTATGACATTTTTTGAAGAGTAGTTTAGTTTTATTAACCAAGAAAAGCC
TCAAGTGAACCTTTAGTCTCTTGATAGCTAACATTTATTGAATGCTTACT
GTGTGCCTGATACTTTTCTGACTTGCATTACCTCACTGAGTCTCACAAT
CTTATGAGGCTACTATTAGTAGCCCCACTTTACAGATGAGCAAACTAAGT
CACAGAAAGGTTAAATAGGTCGTATAGCTATTAAGTGACAAAGCTGAGAG
CCTGTGATCTTAACCACCTTTGGTATGCTGCCATGAAGTTAAATAGCTCAG
TAGTCATTAAAGAGAAACATTTGCATTGAACCTTCCAAGCCACTTAACAA
GTATATGCTTCCTAATCAATTTAATTTAGCTACATTAGATAGAATGGTAA
AGGATCCTTAACTTAAAGTTTAAATGGAAGAAATTAGCCCTCTGAAAGAG
GCACAGATTATTCATCTGCAATAAAAAATCTCACCTTTAGTTTTTAAAC
ATAGTTTTTATCTGTGTTCTGAAATGTAACATAAAACAGTGCTTCTGAAG
TGAAAAAATCTCACTGGTGAGAAATTTAATAAGTTTAAATGATTCACCAA
ATCACTTCAGTCATATTTCACTCATATGCATATGCATATATAGACATATA
AGTTTTTATCTGTGTTCTGAAATGTAACATAAAATAGTGCTTCTGAAGTG
AAAAATTCCTCACTGGTGAGAAATTTAATAAGTTTAAATGATTCACCAAT
CACTTCAGTCATATTTCACTCATATGCATATGCATATGTAGACATATATA
TGTTGTATGTATACATGACATCATTAGACACTGTGAAGGATAGCAAAATG
TATATAAGGCAAAATTTATGAACAATGGTTTAAACGTTTGGGAAGCACTGG
GTTACACTTTTACTTTATGCAGATTGAACCAGTATAGTATGCAAGTCTTA
AGGAAAAATCTACTGGAAAGGGCCCTCATTCACTTCCCAGAGGCTTCT
CTGGAAGTTGACAATACTGACTTCAGTACATCAGCTCGTAAATGAGGATG
ATACCTACCTTATCTGCTTTACACAGTTGTAAAAGTAAAAGTGAACCTCA
GGAAGGGAATTACAGAATTTAGGAGAACTAAAAGCAGATGTAAATAAT
AGTCATCATTACAGTTATATAATGCTTGACAATTTATATAACACTTTTGA
TACATGACAACAATAACTAACCCAGACATGTTTATATACATTACCTCA
CTCAGAACCAACCATGTGAGGAAGTTGGCCATATGCTTTAATGTCCAAACC
AGGACACTTTTGAAGTAAAAGCAGTACTCTTTGACCAACAGGCATAAA
TCAAACTATCTTGTGAAAACCGGGATATATGGCATCCTTCTAGATAAT
AGATACTTTTACTATTATTAATTTTGTCTGTGAATCTAAACCTGCTCTAAA
AAAGTTAATTTTAAAAAGTAATGAAGTACTGATACATGCTACAACATGGG

FIG. 3 (6 of 52)

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TAAATCTTGAAAACGTTATGCTAAGTG...AGAAGCCAGACAGAAAAGG...
ACATATTACATGATTCCATTTATATGACACATCTAAAAATAGGCACATCTA
TAGACATACAGAGACAGAAAGTAGACTAGCGGTTGCCAAGAACTGCAGGG
AGCAGAAGATGGGGAGTGAAGTCCCAATANGAAAACGCATTACGT
>Contig18
TGAATCGCAATGATATGTGCCACTTTGCACTCTCTGTGACATATATAATT
ATTTTTAATGCATTTCATTTTTCTCAGAGTGCATTTCGTTTGAAAACATA
GACGGGAAATACTGGTAGTCTTCCTTGTCAGTTAGAAAACCCAAACAAT
GAAAAATGAAAAAGTTGCACAAATAGTCTCTAAAAACAATGAACTATTG
CCTGAGGAATTGAAGTTTAAAAAGAAGCACATAAGCAACAACAAGGATAA
TCCTAGAAAACCAAGTTCTGCTGACTGGGTGATTTCACTTCTCTTTGCTTC
CTCATCTGGATTGGCATATTCCTAATATCCCTCCAGAACTATTTCCCT
GTTGTACTAACTGTGTATATCATCTGTGTTTGTACATAGACATTAATC
TGCCTTGTGATCATGGTTTTAGAAATCATCAAGCCTAGGTGAGCACCTT
TTAGCTTCTGAGCAATGTGAAATACAACCTTTATGAGGATCATCAAATAC
GAATTCATCCTGAATGACGCCCTCAATCAAAGTATAATTGAGCCAATGA
TCAGTACCTCACGGCTGCTGCATTACATAATCTGGATGAAGCAGGTACAT
TAAAATGGCACCAGACATTTCTGTATCCTCCCTCCTTTCACTTACTTA
TTTATTTATTTCAATCTTTCTGCTTGCAAAAAACATACCTCTTCAGAGTT
CTGGGTTGCACAATTTCTCCAGAATAGCTTGAAACACAGCACCCCATAA
AAATCCCAAGCCAGGGCAGAAGGTTCAACTAAATCTGGAAGTTCCACAAG
AGAGAAGTTTCTATCTTTGAGAGTAAAGGGTTGTGCACAAAGCTAGCTG
ATGTACTACCTCTTTGGTTCTTTGAGACATTCTTACCCTCAATTTTAAAA
CTGAGGAAACTGTCAGACATATTAATGATTTACTCAGATTTACCCAGAA
GCCAATGAAGAACAATCACTCTCCTTTAAAAAGTCTGTTGATCAAACCTCA
CAAGTAACACCAACCAGGAAGATCTTTATTATCTCTGATAACATATTTG
TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTTAAAGGATGAAGTTT
AGTGTCCAAAAACTTTTATCACACACATCCAATTTTCATGGCGGACATGT
TTTAGTTTCAACAGTATACATATTTTCAAAGGTCAGAGAGGCAATTTTG
CAATAAACAAGCAAGACTTTTTCTGATTGGATGCACCTCAGCTAACATGC
TTTCAACTCTACATTTACAAATTATTTTGTGTTCTATTTTTCTACTTAAT
ATTATTTCTGCAATTTTCCCAATATTGACATCGTGTATGTATTTGCCATT
TTTAATATCACTAGACAATTCATCAGGTTGCTACGTTGGTCCCTTGGGT
TTACTCTAAATAGCTTGATTGCAAATATCTTTGTATATATTATGTTTTT
TCTCCTATCTTGTAATTTCTTTGAGCACATCCCAAAGAGGAATGCCTAGA
TCAATGGGCACAAATAATTTGACAGCTCTTATTAACATTATTCTGTAAAG
TAAAAACTGAACTACTTTTCAAGTATCACTAGCAACATATGAGTGTATCAG
CTTCCTAAACCCCTCCATGTTAGGTCAATTATGAACCTATGATCTAACAA
TTACAGGGTCTTATCCCACTAATGAAATTATAAGAGATTCAACACTTATT
CAGCCCCGAAGGATTCATTCAACGTAGAAAAATCTAAGAACATTAACCAA
GTATTTACCTGCCTAGTGAGTGTGGAAGACATTGTGAAGGACACAAAGAT
GTATAGAATTCCATTCTGACTTCCAGGTATTTACACCATAGGTGGGGAC
CTAACTAC
CATGCACACACAATCTACATCAACACTTGATTTTATACAAATACAATGAA
TTTACTTTCTTTTGGTTCTTCTCTTCAACAGTGAAATTTGACATGGGTG
CTTATAAGTCATCAAAGGATGATGCTAAAAATACCGTGATTCTAAGAATC
TCAAAAACCTCAATTGTTTGTGACTGCGCAAGAAGAAAACCCCATGCTG
CTGAAAGTCAGTTGTCTTTGTCTCCAACCTTACTTCTTTACCTCTCAT
ATGTTTGTGAATAAGCCCAATAAGCAGACNCCTCCTACAAAGTGAACCTG
GTCTCTTCTCTCCTAACAGGG
>Contig19
GTCTTGTAACACAGGTAAGACGAGTTCAAGTTTTATTTCTTGNTTTTAGA
ACGGTAGTGAGCGGTTTTGAGCAGTACACCTAAGGTAAGTAGCTG
AATTGGGGTTTTGTCTTGGCTAAAGTTTAAACACAGCTGGTCTTAATTT
CTCCTTACCATTAGAGCACTCAGTAATCATATAAGTTGTGTGATCATTCA
TTTTGCTTAACTGTTTGTCTTCTGTTTTATTGCTGTTTCAGTCTTTTCC
CATTGGGTTTGACCTACTCTATCTGACTTGATCAAATCCAAAGGAAATTT
CCAAATTATGGGGAATGAGGCCTCTGAAGTGGCTAAATCCCACCTCCC
ACACACACAAACGTGGTATGGTGGGGGAAAAACGGCCAGCAAAAGAAAA
AAAAAAGGAAAGATGTTTCATTTTGACCACCAACGGGCTTTATTTAC

FIG. 3 (7 of 52)

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ATAACAAGGCCACCTTT...GCTAGCCA...CCATACTGAAAGAGCAATG...
TGTTGCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTTCTCCTA
CCACGACAGCCTGGGTTTGGTTCCCTAAATCAAGCCTTTCTGGTTTGATA
CTTGGAATGCTGAAATAGCAGCAATTTGTCTAGCTGAAATATCGTAAT
AAGATTTTAAAAGATTTATTTTAAAGGACCTCAATAGTTAAAAGTCAGCT
TAATTTAAAGCTAACATCCAAGATGTGTGCATGTGTATGCGTCTTT
GTATTTAAATAGCCCTCATGTTTTTTTTTCTTTCTAGGAACTTGCCTT
TTTTTGAGCAAAAGTTTTTTTCTTCTGTGACTGGATTCTGTTTTCTT
CATTTACTTCTGCTGTCTCTCCTTTCTCTTGACCGTCTGCTGCATGAGA
GCCCTAAAATAGTTTATAATAGCCTGGGGTTCCTTAAAGAAAATGGAGAA
GGTGCCAGGCTCCCTTTTAGGGAGAACTTCTATTTTTCTTATGGAATC
CCTAGAGTGTAAACAGACAAGTTCATTCAGCTCTTAAACTGCTTGCCTT
TGTGTTGTGTACCTGATTTTTTTGACTATTATTTTTGACTAGCTATT
GCAACAGAAGCTACTCTTGGGTTTTCAAGGAAGATTGTAGTTTAGACATG
TAGAAATGTCTTTAAAAAAAACAACTTTTTTTTAAAGTGCCTGTAA
AAGCATCATATGGTCTAGCCTCCTAATAATTTTCCCTTTTTGGAGACCAG
GATTTCAGGGTGGGCTCTGCCCAGAGCTCAGAGATCCAGTTAAAGAGAGG
TAGTCTCGGCGGGCGTAGAGGCCAGCCTGTAATCCAGCACTTTGGGA
GGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCCA
ACATGGTGAACCCCGCTCTACTAAAAATACAAAATTAGCTGGGTGTG
GTGGCAGGTGCCTGTAGTCCAGCCACTCGGGAGACTGAGGAAAGAGGAG
AATCGTTTGAACCCGGGAGGCGGAGCTTGCACTGAGACGAGATGGCGCCA
CTGCACTCCAGCCTGGCGACAGTGAGACTCCGTCTCAAAAAAAAAAAGAT
AGGTAGACTCGATGTTGTCTACCCGAGCAAGTTAGAGCAACGCCACACT
TTGAGACGAATTTAAGAGTCTTTATCAGCCGCGGACCAAGAGACGGCTA
ACGCTCGAAATTTCTCTCGGCCCTTGGAAGGGGCTGATTTTCTTTTATG
CTTTGGTTTAGGAAGGGGAGGGAGCTCAGTTGCAACAATTCTACAGGAG
TAAAAACATGCAAAGAAATTAAAAAGACAAGTGGTTACAGGGAACAAAC
AGTTCCAGGTGCAGGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG
GCTCTGCCGGACACAACTCAAGGCTTTATGCTGTTATCTCTTGAGCGAA
ATCCTGGGAACCTCGTACATTGCTTGCTTCAGTACCTTATCAGTTAATCG
GACTCTTTGATATGTTGGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA
AGGGGGTGGGTGAAGGAGTCCTTGATGTCTGGTAAATGAAGGAGCGAAATC
GAGTTCTCTGGCTTTCTCAGCTAAGGGAGAGCTTATTCATGTGGAACA
AGGCTAAGTGATTAAGGGAGAAAGGGAGAGTCTGAAAACAAGGTTAGGTA
TTACAATGTCAATAAAATTGGTCTCCTTATACAGTCCCTATGGTAGATTC
TTTCCATCTTTAATCTCCCTCTAGCACCACCAGACTTTTTCTCTCTGTAC
CTTGAGATGTAAATTTTGCTATCTGAATTTTCGTCTAAGAGTTGTTTCTT
TTAATATGCAAATTTAGGGTTATTTAGCTGACAACTGCCAAAGTAGTGAA
ACAAGTTTCAAGAACTTGAACGTCTAAGGTAGGAAAAAAAAAAGTCTTT
ATGAATCTATAAGATGTACTTCTATTGGCATGCCTAATACGTCTATGTAT
TTACGTGTTGTGTACACAGTTTTTCACTACTGAAAATATATAGAGGAGTT
CTAATTAATTGACTTAAGACAATAAAAGCGCTTGAATCAAATACCTTATC
AGGAAAAAGGAAAAAGACAAGTCAAATGCTTGTTCAGTCTATATACTTA
AGTAAAACTTTAATAAATAAGCTAGCTTTAACATTATTTGAAATGTCTT
AAGAATTGCCAGCAGGTTCTGGGTTACAGAATAGTGGGGGTGCAGTGGG
GTGAGGGTGTGGTGGGGTGGGNGGTNNNACNNNNNNNCCCCCCCCCCCCC
CCCCCCCCCCCCCTCCCCCCCCCGCCCCGNGCGGGCCGCGCCCCCCCCCGC
CCCCCGGCCCCGCCCCCGCGCCCCCACCCCCCCCCCCCCCCCCCGC
GCCCCGCCCCCCCCCGCGCCCCCACCCCCCCCCCCCCCCCCCGCCCCC
CCCCCCCCCCCCACCCCCCACACCCGGCCCAACGCAACCCCCACCCCGAC
GCCCCGCCCCCCCCCCCCCGCAGCCGACGCCCCCCCCCCCCCGCCCCG
CCCCGACCCCCGACCCCCCCCCCGCCCCCCCCCCCCCGCCCCCCCCCG
GCCCCCCCCCCCCCGCGCGCGCCCCACCCCCCCCCCCCCAGCCCCGACC
GCGCGCCCCCCCCACCCCCCCCCAGCCCCCGCCCCCGCCCCGACCC
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GGCAGTACGCTATAATTCCCTCTTCACCTTACCTCATCTGTTCTCTGATG
GATGTACTTTTTTTTTTAGTTTCTAAATTCCTTTTCTTTGCTCTGGAG
ATGGGTGATTGATGTAGTCTGGGTATTGTTCCCTCCAAATCTCATGTTG
AAATGTAATCCCCAGTGTTGGAGGTAGGGCCTGGTGGGAGGTGTTTGGAT

FIG. 3 (8 of 52)

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CATGGGGGCGAGATCCC. ATGAATAGC. GGTACTGTCTCTCAATAG. 4
AATGAGTTCTCTGAGATATGGTTGTTTAAAAGTGTGTGGCACTCCCCCA
TTGCTCTCTTGTACTGCTTTGACATGTGACATCCCTGCTCCCTTCGC
TCTCTGCCATGATTGAAAGTTTCCTAAGGCTTCGCCAAAAGCTGAGCAGA
TGTGGGTGCCATGCTTGTACAGCCTGCAGAACTGTGAGCCAAAATAAACT
TCATTTCCATATAAAATTACCCAGCCTCAGATATTTCTTTATAGCAACATA
AGAGTGGCTTAATACAGGCTGGGCATGGTGGCTCACGCCTGTAATCCCAG
CCTGTGGGAGGCTGAGGGGGGTGGAACATGAGGTCAGGAGATTGAGACC
ACCGGCTAACACGGTGAACTCCATCTCTACTAAAAATACAAAAAATTAG
TCGGGCGTGGTGGTGGGCGCCTGTAGTCCAGCTACTCTGGAGGCTGAGG
CAGGAGAATGGCATGAACCCGGGAAGCGGAGCTTGCACTGAGCCGAGATT
GCACCACTGCACCTCCAGCCTGGGCGACAAGAGTGAAGCTCCATTTAAAAA
GAAAAACAAAATTTCAAACAGAACAAAATGAAAAAATACCAAGTGAAA
GGCCCTATAAAAAACCCCTCTGGGGCCCATCTCCCACCCCTCAAGTGA
AACCACATTTAACAATTTGGTGCATATCTTCCAAACCTTTTGTGTACA
CATATAAAAAACATACATGCTTTGATTTGGCTCAGACTGTACATAGTGT
TTCCCTCTTGCAATTTTACACTTAATATATCTTTGACATCTTTCTATGTCA
GTGCATGTTGGCTCGATGATATTCTATCATTAAATACCCCTTCCAAAAATG
GTAAATCATTTTAAAAAATCATTACACAAAGTACATATTTACAATTTTA
AAAGAAAAACAGAAATCCCAAAACACAACGACAAACCTCTAAAAATAATCTC
TATCTTTCACCAGCATGGAACAGTTCATTCTTTTTTACATAAAACGAA
TTATGTGATTGGAAAGATTAACCTAATCTACACATTTATATACAGAATG
TTCTATTTGTTAAGCCTATCTGAAAAATAAAAAATTCAGATGATTAATTCA
CTTACACTTAGAAATTAAGTCAATATACTATGAATACACATTGTGATCAG
TTATAATATGATGCTTCTTAGTCTAGGGTTTCAATTAATAACAGTAAAA
AAAATTGGATAAAATAAGACAGCTAATAACTGAAAAATCCAGAAATTCAAA
GATTATATTGCCAACTAAAACACTGCCATTTACATTTTTTTTTCTACTT
GGTAGCAAATGCTAATGGAATTCAATCCTGATTACTTAAAGTCAGTTCAC
ATCACACATTCATCAGGATAATACGAACATAATATGCCTACTATAGCGT
TAGATTAAGACATAAAATTTTTTGTCTGAAAGTAATGACTGCGTACCAC
TTGAGACATTTGTCAACCACTTCAGCACATTGTTTACGAGTGAAGTGGATG
TCCCAAGGAATAAAACGACAGCAATATTTCTATCCATACAGATTTTGC
AAAGCTTCTCTCTTTCAGGTGTCTTAGCTGCTCTTCAGTACTAATCTCT
TTCTGCAATGAAGTCTGACTTGATTCTGCTTGTGTACTGTCTTTCTGAGC
CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTTACAGTTGCTCCAG
ATGTCTGAATTTTTCTCCATTATTTCTTAATGTCTTTGAAACTGAAC
CCCATTCATATAGCTTCTTGTACCATAGGATTATGGAAGATGGTATCAAT
TTTTCTAGTTAGTGATGGCGTTTTTTTTCAGCAGTTCTTACCAGACACTCCT
CAAGTGAATGGGATAAATGAATATTGTTTATATATTTTCGTGTCTTCTGT
CTAACAGATATTTACACCCTGGATGCCATTAACATGTTGTCCCAAGGGT
CTTNCTGGGCT

>Contig21

CTTTCTCCCTTTTTACCCCATTTTTCGTAGGGATTGGTTAAAACCCATG
TAAAAATCCAAACACCGGCGGGGAACGGGGGTCAAGCTCGTATCCCCA
CCACTTTGGGAACCAAGGTGGCAGGATTGTGCGAAGCCAGGCATTTGAG
CCCACCCCTTGGGAAAAAAGAGAACCCCATTTTTTTGAACAAAAACC
CCAACCCCTCCAGGAAAGAAATAAGTATGGCTGGGTGAAAGTACCAAAG
ATGGCCGACTGGCTGGTCAAGTAACTTTACCTGATGGTTCGTAGAATATT
TACCTTCACCCAGGTGGGAGAATTGCTTGAGCCAACCCCTCAGTGTGGATT
CAGGAACTTGATTTAATTGGTATCGTGATTGTGGATTAGATTCTCAGGGA
TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTAAGTAAAAATAATGA
ATGAATCAAAACACTCTAAATCCATGGTGCTATGCTAAGCTCTTCTGTAT
TTTATCTCAATTTGATATTACAAATATTTGATGTGTTAATAGTAATGACTA
TCTCCATTTTTACAAGTAAGGAACTGACATTGAGAGATTAAAAGACTAG
CACAAATCACAAAGTAAATGAGATTTGAATCCGGTCTTGATTCCAAACTC
TACAGTATTCTAAATTCAAGGAGACTAAATTTATAAGATGGAGAGCCAATT
TTACTTTATAACAGGGTTAGAAATGGCAGAAGAGACCTGACATTCACACCT
CTAGCCAGTGCATCATCTTCTGTAGGCAATATGCAGGAAATCTATAAT
AAGAACGTCCTTTGGTGAAGGCCAGGTGCAGGGGCTTACACTTGTAATTC
CAGCACTTTGGGAGGTCAAGGTGGGAGGGTCSCTTGATGACAGGAGTTTG

FIG. 3 (9 of 52)

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AGAACAGCCTGGGCAACAAGTGAGAC...TGTCTCTACAAACAAAAACA
ACACAAAAACAACCTCAAGAAAACTCCTTTGGTATGGATCAGAACAGATG
AATTATCTATCTGATCCAAATGCTTAATGACATTAAGCCACAGTCCACTC
ACTGCCACAATAGAGATATACCTGCCAATGCCACTCAGGTAATCCCATCA
AAAGTGGTAATGAGGTCTGCAGCATGACTTGTCTTAGTGATCCCAGCCT
GAGACCTTGAGATTGCAGCATTTTATTCTACATATGCACAAAACATCTGT
TGAAAAATCTTCTAAATTGATGCAATACATTTCGTATCAAGAATACCTGTC
TGTAATCTCCATAAACCCCTCTCCTTTCTGTTTTAAAAAATAGTAACAGCA
TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGAA
TAGGAGCTGTGTGGAAGGAAATTAGCTCTACTTCTTGGTGGAGATGAGAA
GGGAGTGTTCCTCTGAAAATCAAGGCTCTTGTCTATGCTAGGAGCCAAAGT
CGTTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT
CATGTTTTTCTTATTCCATAGGCCTCTCTCAATTGGGCAAAGCACTCCAG
ACCTTTTGGAAAGAGTGACACCAAGGCAAGCACCTGCTTGGCAGGCCCT
CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT
GTTGAGTACCTTATTTCCAAATGAGGCTGCCGGTGTCCCTGTGGCTGTG
AGAAGGCCTCTACTGGATAGGTGGAAGTTGTGTGTTCTCATCTTTTCTAA
CCCTGGATTGACTTGCCCAAAAGGAAGCCATTATTAACACTATAATAAAA
CCATCCTTAATCTGGGACTCTCTTCATGCAGTGGTTCTTAACCAGTGATA
AACATGAGAGTTACTTTTGGAGCTTAAAAAAATTAAGATGCTCAAGGTCT
ACCCAAACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGTATACTTTT
GAGCCAGACCTCAGTTTACCCTGCAGAGCTCATAAGGTGCATAACACCC
TTTGTGAGCCACTCTGATGAAAAGAAAAATTGGTGAGGAATAAGTTTAG
AGAAGAAGGAGCAAAGGTGTTCTTGGCCAGTGAGAGCCAATGACAGGGAA
ATGCAACAATGTATCCACAAGAAAGGTAAATTACCCTATAGAGCATTTT
AGGATAAATGAACATCTCATGCCTAGGGTTGAGAGAGGGTACAAAAAAA
AAAAAAAAAAGACCACTCTGGATACACAACGCGATAAATGGAATAAAGAA
TTTTTTCCTTGTAATTAAAAAATCCTTTGTTACTGAGGTATAATTTAA
TCTATTTTATGTATAGTTCAATGAGGTGTTATAGATAATAAATTTTTTT
GTAAATTATTATATTGTATATACTCATACATTCTTTTAAAGTCAGA
AATGTATATAACCATTAACCTTATAAATCATTGAGTCATTGAGAGATATA
GATACACGAGCATATTTTATATCCACCACAATAATTATTACCATCTCAAC
AATTCATCACCCCTCAAATTTCAAGCGTAGGGGTTTTTAAATGTCAAAG
GAGTCTACTCAGTGGGAAGAAAGTTAAGGAAAAAACCTTTGGGGCTTTGG
GCTCCTTCCCCCTGGGGTTAAAAAGGCAGGAAATTGGGCTTACCCCCCT
GAAATTGGGAAGTTTAAAAAAGGTTTAAAAAAGGTTTAAAAAAGGTTT

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TCAAGCAGCCTTCCTTCCTTGGCTTCCCAAATGTTGGGATTACAGGCAT
GAGTCAGGATTCTGGCTTAGTTTACATTTCTAGAGTTTTGTATAAATG
GAAACATACAGAATGTATTTTTTGGCGAGTGGGGAGTGTCTATTTC
TTTCTTTCCATTTTCCCCCCCCNCCCCCGAGACGGAGTCTCGCTCTG
TCTGTTGCCAGGTGGAGTGCAGTGGTGCGATCTCGGCTCACCGCAAGC
TCCACCTCCCGGTTCAAGCAATTCTCTGCTCAGCCTCCTGAGTAGCT
GGGATTACAGGCGCCGCCACACACCTGGCTAATTTTTTTGTATTTTT
GGTAGAGACGGGGTTTACCATGTTAGCCAGGATGGTCTCGATCTCCTGA
CCTCGTGATCTGCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACAGGCGT
GAGCCACCGTGCCCGGCCCAAGTGTTCATTTCTTAACCAGCTTTCATG
CAATCTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGGTACTA
GATGTCGATTGGTCCTTAGGATCAGCTACCATTTGCCCACTGCTTTCCA
GCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTGTGAGG
CTCAGAACTCTGAATTGCTACTGCAAAATATGAACTCGGTGATGTGAATG
CCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCCTCACT
CTTGCTGTCTTCTCATTTGTTTTCCCATCCTTGTGGATTCTGAATTTA
AATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAAGTACA
GAATTAGGTGCAAGAGTGCATAGCTGTTATTTTTTTTTTGGCCTCTGAGA
CTGTTTATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACCTGAGA
TGTCAGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAAAAAA
TAATGCCATTTCTGGTTTGTACTTCGGTAAGTTCAGATGACCCAATATAT
TGTTTACATGTGGCATTGAGTAAAAAGTAGCTTCCCTCCCTTTCTTCT
TCCTTTTCTCCTTCTCTGCTTCTATAAAGCATCTGCTTTGGGAAACTTCT

FIG. 3 (10 of 52)

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TAGGAGGAGAGCTTGGCCAGCCCGTGGC .ATGGAGAGGTCTTGCAGAGA.
AAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATGGGGAT
ACGTCTGGCATCACTCAGGAATGGGCCTTCTGGCAGGGAAAAAAGGGA
GGGGAAGAGGAAGGGAATTCNNANATNAATTGCTGAATACGGGGATTCC
ATGGCCTGGATCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAAGGCA
TCANCTGATGAGGAGCAGCCTGAACTCCGGGGAGGACCTGTTTTTGGTGG
CCCCGAAAAAATGCCTTCCACACACAGGGAGGCCACCCGGCTGATGGGC
TGGGGGTGGACGGACAGCCCTAGGACAGGCTTGGGAAACCAGGCTCAGG
TAGGGCTGCGAGGTTCTCGCTGCGTCTCTTTCTTCTGCTGTTAGAAA
ATAGAAATCCAAGGCCTCTTGAGAGTGGAAAGGTGGGTTGGGAGGAGGGCAG
ATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCTCTC
AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAGACA
GTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCTTCTCTTTCAAT
GAAAGTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAATAT
TCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCCAACTTCC
TGTGCTGGGGAATCCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGACAA
AGTGAATTCGAGTGAATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA
GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAACCC
AGAATTTCCCGCACGTGTCTCAGGCTCTCATTGCCAACTCAGTCTCTA
AGTATTTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGAAATAATTCA
TTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGACTCTCTTTA
CCTTTCCCTGGGATGGAAGATGCAATGTTCTGATCTCACTGTCAAAAA
AGAAGAACCAGTGGGTATATTGTATGCTTGAGTTCAGCCATTAGTCACA
AGACATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGACTGTGTGCT
AAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATGTCCATGGTCT
GGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTCATTTTCTGT
GGAGGGGGTGTATGGTTAAAGGAACGGCTGGGATTTACTCTTCTTTCTAG
GGCCAAGAAAAATGACATGCTGCCTCCATGTTTAAATCATCCTTCCCGCTGT
TAATAACTATGGCTTTAAGTCCCGGTTAGGGCTTCTTCCAAAAATTGGG
GAAAAAAATTCCTTCCCGCTTAAAAATTTTTTTTTTAAAAAACCTTT
TTTTTGGGGGTGGGAAAAAACCAAAATTTTTTTTCCCAGGGGTTT
TTTAATTTAAATTTCTCCCCAAAAATTTGTTTTTTTTTCCGCGAAAAA
AAGACCCCCCAAAAAAAGTTTTTTGGCGGAAAAAATATTTTT
TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTTTTCTTCTCCCCC
CACCCGCCAAAGGAAAGTTGTTACAGATTGTTTTGTGTCTCCCGCCCA
T

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ATGTGCCTGCGAAATCATCCTTCCAGAAATATTTGCCCTTTCTTTTGT
ATAGAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTG
AACACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAACACAT
ACCAAATTTCAAAGACATGGCACATAATAAAAAATGTAATAATCTCATT
AACAATTTTTATATTGACTGTGTAAAGTAACATTTTGAATATATTGGATTA
AATACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACT
TCACATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCT
ATTAATGTGCTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAATGAC
ATATAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTG
CTGCATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACTATCAGTGACAT
TTAGTGAGGAATTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTAC
TTAATTCCTCTAAGCCCGGTTTATATCCCTGCAAAGAGAGAAGGATAATA
ATCACCAGTACTTAGTGATGTGTAAGGAGAAAAATAAATAAATATG
AAATGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAG
CTGCTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAA
TGTGATGGTGCAGTACATTCAATGTTGGACATGGGTGAAGGAAAGAC
CAGGCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGGAGGAATC
AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGG
CACACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAG
CTGTGGGTGGTGGTGAAGTCAGACCCAGCTTCCCTCTGTGCCTGGCTGAGT
GGTTCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCATCTATAG
AGAGGGAGCAACTGAGGCCCCCTTCCAATACTGAAGTCTTTATTTCTGCT
ACTTTAGAAATATCCACATTTTGGTAAATCAAATGATCCAATGATTCC

FIG. 3 (11 of 52)

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ATTTCTTAATGTTCAAAAAGAGCCCAACACATCTAAATGAATCAAC
 AATAAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGC
 AACACACACACACACACAGAACCCATAAGCCTTCATCTTCTTGGAT
 AAACGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATT
 CCAACTCGCCTTTTGCAGCAGTTTCAATGGGTCTTCTGCGTGGCAGTG
 GCCCTCTGACTTATGATTTCTGTGTGTGGCCTGTTACCACTGCAGCT
 TAACTGAGGAAACAAGAACAAAACAGCCTCTGACCCCAAGAGACTGTTGG
 AGGCAAAGGCTTCAGTCCCAAGAACCCTCACACGTGGGGAGCCCGAGAGCC
 CAGCCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGC
 CTTATTTTGGATACAAAGAGTGGTGTCTTCTTAAATCTTCTTTAGTC
 AGGGGTACCCCTTCATGGACGCCCAACATCCATGGTTCCTGCTTGAGTC
 CCTGCTTCCATATTCCTGCACTTCTCACTTGAAATATCCCTGGAGTACGT
 TAAGCAGCCAGGTTTGGAGTTCTTGCTGTGCAGGCGGGTGTGTGCATGT
 CCTCTCTCAACAGGACAAAGCTCCCAAAATCAGACGGTATGCCTCCA
 CGCCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGG
 GGCCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGATGC
 GCCCTCACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGTTTTT
 CCTCTGGACAATCAACATGAACTCCTCACCCTCTTATCCACTTTGCAT
 AAATGAAAATAACAAACCCAGGGTCTTCTGTACAGGAAAGGGTTTTT
 TTTTATAAGATTAAACAGAGATGATTCAACACACCCAGGATATAACACAT
 GGGCCATGAGTCAAGGCCAGGCATTGCTCTGGTCAGCCTGTTGTTGGGC
 CCCCTTGGCAGGGCTCTCCCCCTGAATCTTCCCCCTTGTACTCCCCATCA
 CCACAGCACGTCCAGCTTTGGGTACAAGGCCAGTAAATGGGGAAGGGGT
 CAGATGACATAAAGAGCCCTTCTGTCCCATTAATATATTTGGATAA
 CAGATGGCAATTTCCCCCTGTGTCTTGGCCAGGGCCAGAGCCTCCACTTG
 CTAGAGGCAGACAGAGGATGGAGAGCCCTTCATTAGTGGGAGGACATCA
 CAGGTGGGCAAGAAACCACAAGCTTGCCTGAGGCCAGCCTTGAAATAG
 CAGCACCTGCGCGCAGCTGTGGTCTGGGGACAGGGTACAGGATGGAGGG
 GCCTCCTAAGCCTTTTATCTCTATGTACTAAGTACAACCCATTTTCCAC
 CTCACAGAGCCAGATCAGCCTCTGTGAGGTCTGGTGGCAAAGGATAAT
 TGCCTGCCCGCTGCCCGCGTGGGTGCTTGTGCTTGCAATCCTGGGAA
 GGTGTTGGGTTACTCTGCAATAGGTCTCTGACCAGCTCACCCTCCTA
 CTGCAACCTCAAACCACTTCAAAGAAGATCCAGCACC

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CGCGTAGTCTAAAGACTGAGTCTGAAGCTGTCCCTTCTGCTATGGACTT
 CAGATTTTAGCCCACTTGAATTGCTCCATATCCTCCAAGCCATGGCCATC
 CTTGACTCTCTGGGCTCCCAAGCACTTGCTGCCTTCATCACACAGTTTG
 AGTTAAGGCAGAAAGACTGGTTTCCATGTACACTTTGTGGAAGCTTCTC
 ATTTCTTATATAATCTCTGTCTTTGTCTACTGCTTTAAATCTAGAAA
 TTGTTTACAAACAAAGGTGATCCTTTAAAGCTCAAAGCTGATTGTGT
 CACCAATATATACCACTCTTAATGGCTTCCATTAAACTTTGAGTAAAGA
 CTTTATGGAGCCTACATAAGGCCATGACTACCTGGCTCTTATTTTCTCC
 TCATCCTCATCTACCAACTCACTCTCCACTCCTATACCCCTCACTCCTT
 CCCCCCTCTCTCTGAGCTCCAGACTCCCAATTACCTACTTCCACCCTT
 TTTGACCCCCAGGCACTTATCTCAGCCTGGAAATTTCCCTCTTTGCTCTC
 CACTGAACTGTCCACTCCCACTTAAGACATGTGCTTATGTACACGCCCC
 TTACCGTGCTTATCTCAGTTTGTAAATTATCTACTCATTTAGAAAAGTGT
 GATGAAGGCTTCACTGTGAGCTTTTCAAGGATAGCAGGAATCATAGCTGAT
 TTTACTTACTTAACGGGGTTTCAATCTTTGTAACTTTTTTTTTTTTGGAG
 ATGGAGACTCACTCTTGGCCAGGCTGGAGTGCAATGGCATGATCTCGGCT
 CACTGCAACCTCCACCCTCCTGGGTCAAGTGATTCTCCTGCTTCAGCCTC
 CCGAGTAGCTGGGATTACAGATGCCTGTCAACACGCCAGCTAAATTTTT
 GTATTTTTTGTAAAGACGGGGTTTTCATCATGTTGGCCAGGCTGGTCTCGA
 TCTCCTGACCTCAGGCGATCCACCCACCTCAGCCTCCCAAAGTGCTGTGA
 TTACAGGCATGAGCCACGGCACCCAGCCACTCTTTTTTACTTATGGGTG
 AGAAGCCATTAGAGATCAATTTCTTTCTTTCTCTCTTCACTAAGGCA
 CCAGGGTCACTAAGTAGTAGGATACTTTGAACTAGAACTCAAGAAATTGA
 GTTTTAAATTTACCTCACACTCTCATATGAATCTCCATGTGACCTCGGG
 CCATACTTCCCTGTACCTGTTCCTCTTTTATAAAAGTAAGAGTTTAA
 ACTAGATGGTCTCCGACATGCATCCTTCTCTAACATATTCTGGAACCTTC

FIG. 3 (12 of 52)

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AATAAACTAAGATAAAC .GAATAATTAAACTTAATTTAAAAGAACAA
GGAAAGGAAGCAGTTACATTAAGCAAAAGAGACATCTTCATGGTTGAAGA
AGTGTATGCCCTGGTGTCTGGATCCCATTTAGGAACTTGGTAACCTTGC
AATCTTGGGCAGATTGCTTAATTTCTCTAGACCATGACTTCCTCTTCTGT
AAGATGTGATAAGAACATCTACCTCACAGGTTTCATGAGAGGATTAAATG
AGATAATGTATTATAATCCCTTGAACATGGTAGGCTGTTATGTTAAGTCC
TTTCCTCCTTCTCTGTAGCTATCATGGAATTTAAAAACACATTATAACTA
GAGCATGAGTTGCGACTAAAGGCTCAATTGTCTCTGCATGTGTTGGCTCA
TGCATGCTTTATTCCTCTGAAGAGCTTTTATACCAAGTGAAAGGAAATAA
TTGCATTTCCCTGAAATTCACAGGAAAAAGTTATGTTTTCTCTTCATT
CAAGTGATTCTGTTAGACCCAACCACATGCAACAATTTTAAAGTTGCTTC
CAAATATATTTACAAATATTTCTGTCTTCAAGGAACATGGCAAGACCA
TGACTCAGGTTTACATCCGGATTCCACCCTAACCATGTACCCAATTACT
TCAGTCACCTTCATTGAGGCTTACATATCACAGAATAAAATCAGATTTC
ATCAGAGGAGGTGAAGACAGGGAGAGGAGATATTTCAATCCCTTCTCCGC
AACCCCGTTTTTTTTTTTTTTTTTAAACAAGGATCCTAGAGTTACTGAATG
ATAGCACGTTTGGGGGAAAGACCCTAAGGATGATCTTTATAAGCCATC
ACTTGGTGTGGTGGTGATAAAAACTCGAGTATCTTTATGCAAGTGGAAA
GAGAAGATTGGACTCGGAATCAGAAGCTTGAGTTCAAGCACTGGTTTCAT
CAGTCTTGTGATCTTGGGTTGGTCACTTAACCTCTTCAAGGCTCCTCAGC
TGTGAAAGAAGATAGTATCAGCTAATTCTTGTATGTGCAAGTGGAGGCA
GTGAGATAGTGCAGGTAACTATAAAACAATTGTACATGAAACGCATCA
CAGTGATCTTTGGACCCACAAGCTCCAATCTTATAAAACATATCCAGTC
ACCCACCAACATAGATCATCTCACCTTGCAATCTGATTTTGTGGATCAT
GGGGAAAACTGCTGATTCTAGCAAAACCCATGGCATAGGATAAGTGCA
CAATAATTTTTTTTTTCTTAAATGATTTAGATGACAGTGACTCATTAAAGG
TTTCCTGAGGCCTCCTCAGAGTCGAGAGGTGGTGCCTGAAGCCACCCAA
AGTCCCTGTACAGGATGGCTCCCAACGCACACACCACAGGCCTGCCAG
TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCCACTGTC
CCTTCCCTAGAAGAGGTGACTGTTGTTACAGTCCCAGAAAAGCGGGCTC
CCCAAAACAATGCAAGGACCCACCTCTCTCTGAACCTCACCACCCTAGT
TTTTCTTTAAAAATCAATTTACAAGAAGATCATGTGAAGGAAAAGGTTGG
GTGATATTCTAACCCAAGTTAGCTGTTTCTCAACCAAGTTCTCTTTGAAA
AATTCAACAACCACTTTGGGGAATTATTTACAACAGAGGAGTGAGGATG
GGACCAGGATAGGTATTGCCTATGTTGGTGGAACAGGGTTTTTTTCTG
GATTACCAAAAGAGATGGTATGCATTGCTCCCAAGCTAAATATCTTCAG
GCTTTCAATGGTGGCCTTCACTGAAAATGTTATCCCTGTTGAAGCTTTC
AAGCCAGTATTTTATAAGAACTATATTTCTTTGGTGAAGTGAAGCATT
ATAATGATGACTATACAGGTTCTTGAGTGACTGAAGCCATCATTAGCATT
GTCAATATTTTTGTTTAGTTGCATCTCCATAGCAGCTCACATTACAATG
TGCTTTGCAATTTCTTAGCAATAGCCCTCACAAGATTCTCAGGAGGA
GAGGGTTAATCCGATTAAACATTTCTGTGAAGCCTAGCGAGATTAATCGC

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AAGAGTTTTAAATTAAGTAAGGACGCCGGGAAACAAATCAATCCCAGCA
AACATTTTGTGGGATTTATCATTCAAGCAATTTTACAGTTATCCCTGTC
AAATACATTAAGTGTTCAAAATTGGGCATAGGGGGAACAAAATAATAAAC
CCAGCCAAAAACAGAATAATCCCTGTTTGTTCATGTTGGATAAAAAAGAC
ATTACTATTGGTGTAAGGAAATTAGATACATCTTCCATTATTTAGTAAAA
TTACCATAACTTCTAACTTTGTGGCTTTAGGCAGTCTAGTCCACAGGCAG
GAAGGAGGTTTGTGGGCAATGACTGTTATCATCTTCTGTTTCAAAGC
TAAACCATAAACTAAGTTCCTCCCAAAGTTAATTCAGCATATGCCAGGA
ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGGAGTCAGGTAGGTC
AGATCTTCTTCACTGTCTCAGTGATGGCAGTTTCATAACTTTAAATGATG
GCTATCACAGTTTTTATAAATAATCTAGATAAACAGTTAAAAATAAATAA
TTAGGTAAATGTAGTGCATATAATATTAGTAGACAACTCACCATAATTT
AGAATCTAAAGTTAAATTAATAATAATATTTTATTATTTGGTATTTTCC
AAGAAAAACATATTGTAGGAAACCATTCTTTTTAAAAAAAAGTGTCTT
TTTTAAAAAGGTGAATAATTTTTGTCTAATTCAAAGTTTATTGAAAAGTTA
TGTATAAAACAAGGTAAGGAAACAAGGAAATAAGGGAATGTAAAGAAA

FIG. 3 (13 of 52)

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ATTATAGAAATAAAAGTGGTATTTTTTGGTAAGAAAGCTTAAAGAGAAA
ATTTTAGGTAAGAAAGAATCTTACCTAAAATTTTGTGCTAGAATAAAGTG
ACTGGCTAAGAAAGGATGTTCAAAGCTATTTATGACAAACCCACAGCCA
ATATCATACTGAATGGGCAAAAGCTGGAAACATTCCCTTTGAGAACTGGC
ACAAGACAAGGATGTCCTCTCTCACCCTCTTCAACATAGTATCGGA
AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAA
TAGGAAGAGAGGAAGTCAAATTTTCTCCGTTTGCAGATGCATGATTGCAT
ATTTAGAAAACCCCATCATTTTCAGCCCCAAAACCTCTTAAGCTGATAAGC
AAGTTTCAGCAAAAGTCTCAGGATACAAAATCAATGTGCAAAAATCACAGGC
ATTCCTATACACCAATAATAGACTAACAGAGAGCCAAATCATGAGTGAAC
TCCCATTACAAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCTT
ACAATGGACATGAAAGACCTTTTCAGGGTGAAGTGAACCACTGCTCAA
GGAAATAAGAGAGGAAACAAGCAAATGGAAAAACATTCCATGCTTATGGA
TAGGAAGAATCAATATCGTGAAAATGGCCATACTGCCCAAGTAATTTATA
GATTCAATGCTATCCCCATCAAGCTACCATTGACTTTCTTCACAGAATTA
GAAAAAATAAGTCAAGCAATCTTAAGCAAAAAGAACAAAGCTGGAG
GCATTGTGCTACCTGACTTCAAACCTATACTACAAGGCTGCAGTAACCAA
ACAGCATGGTACTGGTACCAAACAGATATATAGACCAAAAGAACAGAAC
AGAGGCCTCAGATATAACACCACACATCTACAACCATCTGATCTTTGACA
AACCTAACAAAAATAAGCAATGGGGAAAAATAATCCCTATTTAATAAATG
ATGTTGGGAAAACCTGGTTAGCCATATGCTGAAAACCTGAACTGGACCCCT
TCCTTACAACCTTATACAAAAATCAACTCAAGATGGATTAAAGATTTAAAC
ATGGCTGGGCATGGTGGCTCAGCCTGTAATCCAGCACTTTGGGAGGCC
GAGATGGGTGGATCATGAGGTGAGGATGGAGACCATCCTGACTAACAC
AGTGAAACCTGTCTCTACTAAAAAATACAAAAATAGCTGGGCATGGT
GGTGGGCGCTGTAGTCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGG
TGTGAAACCAGGAGGTGGAGCTTGCAGGGAGTGGAGATCACGCCACTGCA
CTCCAGCCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAAA
AAAAAAAAAGAGGATTTAAACATAAGACCTAAACCATAAAACCATAGAA
GAAACCTAGGCAATACCATTCAGGACATAGGCATGAGCAAAGACTTCAT
GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT
CTAATTAAGCTGAAGAGCTTCTGCACAGCAAAAGAACTATTGTGAGAGT
GAACAGGCAACCTACAGAAATAGGAGAAAATTTTTCAATCTATCCATCTG
ACAAAGGGCTAATATCCAGAACTCAAGGAATTTAAACAAATTTGCAAG
AAAAAAAAAACCATCAA: AAGTGGGCAAAAGATATGAACAGACACATCTC
AGAAGAAGACATTTATGTGGCCAACAAACATGAAAAAAGCTCATCATCA
CTGGTCATTAGAGAAATGCAAAATGAAACCACATGAGATACCATCTCAT
GCCAGTTAGAATGGCGATTATTAAGAGTCAGGAAACAACAGATGCTGGA
GAGGATGTGGAGAAATAGGAATGCTTTTACACTGTTGGTGGGAGTGTGAG
TTAGTTCAACCATTTGTGGAAGACAGTGTGGCAATTCCTCAAGGATCTGGA
ACCAGAAATACCATTTGACCCAGCAATCCATTACTGGGTATATACCTAA
AGGATTAGAAATCATTCTATTGTAAAGACACATGCACATGTATGTTTATT
GCAGCACTATTCAATAGCAAAGACTTGGGAACAACCCCTAATGCCACC
AATGATAGACTGTGTAAGAAATGTGGACGTATACCCCATGGAATACTAT
GCAGCCATAAAAAAGAATGAGTTCATTCTTTGCACGGAAGTGGATGAAG
CTGGAAGCCATCATTCTCAGCAAACTAACACAGGAACAGAAAACCAACA
CTGCATGTTCTCACTCATAAGTGGGAGTTGAACAATGAGAACACATGGAC
ACAGGGAGGGGAATGTACACACCAGGGCCTGTGAGGAGGTGGGGGGCAA
GGGAGGGGATAACATTAGGAAAAATACCTAATATAGATGACGGGTAAATG
GGTGCAGCAAAACCACCATGGCACATGTACACCTACGTAATAAACCTCCAT
GTTCTTCACATGTATCCAGAACGTAAAGTAAATTTAAAAAGAAAGAA
AGAAAGAAAAGGATGTTACGACAAACCAGAAAGTCCAAGCATGTCTATGA
ATAGTCTGTGTAAGTCACAATAAGAGGATTTATTTAAAAAACTTTTATA
TGATAAAGTTGTCTATAATTAAAGGGAAATTATAATGGTCTTTCTAGAGA
TTGGGTTGATGTTAAAAAACTACTTATATATTAATAAAATTTGGTTAGAACA
ATGAAATTTTCTTACGGGGTTGATTCACTCTTAATAAATTATAAGAGACT
TAAGAATTTTTTTTAAACCAAAGTTTCAAGCTTTTATTGCATCTTGCTGTT
TTAGGTTTTCTCTCCCTTTAAAGGGTGGGAAATAGTAATGCCCTCCTT
CAACTCCCTTCAGCTCATATACGTTTTTACCCTCAGATTCTGTTTGTG
TGTCCTGATGCTAACAAATGTTTTCTTAAAGGTCTAAAGGAAATGTTTTCT

FIG. 3 (14 of 52)

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TCCAACATAATATTCTG1GCATTGCAGAAGGTCTTTTCTTTTGCCCTTTT
GTAACCTGGCTTAACAGATTTTATGTTTTATTGAAATAATTTCTATGCCAT
TATTATTAAGTTTTGGTTTGCTTAGAAAACACTGAGATTAATACAATTTT
TTAAAAATTATGATTATTACATCCATATATCTTTATGTATGTGCTTTTAA
AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGTCTTAAAAGGA
CAAGTCCTGCTAAATCTTAAATACTGACAGCAATTAAGGCTCATCTTCA
GGACTGGTAGAAAATGCCAATCAAAATAAACTGCATTCTTGAAACACAGA
GCCAGAAATTAAAGCTATTCAACTCAAGGCCCAGGAACTATAGTGGAAGA
GGTGGGTGTGTGAGATTGTAAGGGCCAATTTTGAGAGATAAAATAAGTTC
AATTTCTCTATAAATTAATCATAATCATTGATGTCCAAGCCACACTGATG
CAAGATCAGCATATGGGTCTGTGTGAGATTAAACAGGTTTTCTTGAAGC
ATTAACCTACTCCTTAATAAAGGTTATAGAGGTTATAAAAGGCTTCTGGA
AGTTATAGCTATGGTCAAGATAAAAAATTTTATAGATTGTTAATACAATTT
TGGAAAACAAATTTAATTGGCTTCTTGCTGTTTTTATTAGGGCTTATTGT
TTGGAAAATTAAGTCTCGTCTCTCAAAGAATGAAGGCTTTCACCTTTTTT
TTTTTTTTTTTTTAATCCTTGAGTTATCACTTTGGTCAAATGAATGACTTA
TTTTACAATGACCTTTTATCAAGTGTTTTAAACCTTTCAAATTTGACAAA
CTTTCCAAAATCAAATACTACAAATTATGTCTTTTTATGACCTAATGAATCC
TTTAAATACTAGGTTCCCTAAAGTCCAAAAAATAAATAACATAA
TGTGGCTTATTTGGTATAAAAAATTTTACAAGAAACATTGTCAAATATAAA
ATATTGTGTGGTTTTGTTTGGGCTGTATTTGTATAAATATGTTATPGGTA
TGTGTTCCAAAATTATAGGAACTCCTATAATTCTGATATGACTTGGTGT
ACATTATCAGTAATAATTATAATTGTTATGGTAAATATTGTGTGCCATG
GAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTATGGTTGCCCTAA
AACTTTTTGCCATTACAGACAATTGTCTTGCTTTGGTCTCTTTAGAAG
GTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCTCTTGAATGCAGG
CTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAGGAAAACTTTCA
GTATTCATGGAGTGTCTGAAATATTATGAATATCAAGCAAAACAGGAATT
AACTTCATAGATGGAACATAAAGAATGCTGAAGTAATCTTTTTGACTTTT
TTTCTTAGAATGTTGATCCTTCGTTTTGTTTTTTCAGAGTCNAGGAAATTT
TTCTGTTGAGATATTGACAGCTTTAACAATTAAGTATACTCCAGTGAACA
CAATTTGGAGCA

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ATCTAGTCATTCCCCAGCCTGACCAATTCAATGGCCCCCATCTTAGTTAA
AATTCCTCACCCTGACAAGGCCCCATCTACGCCTCTGACCTCATGCCCTC
CACTCTCAGTCTTGCACTCACCTGCCACACTCAAGGGCTTCCCCAGGTT
CCTTCTTAGATTCCACCGATAGCTCAGGGACTTTGCACATGCTACGGTCT
CTGCCTGGCTCCTCCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGC
ACCCCTCAGAGACTGTCCCTGCCCCACCTCTCCAGGTTCCATACCTGCCA
CCCTCCCCCAATCACGTAACAGTTTCTTACAGAGCGAGTTACCATCCCA
GTATTTCCCTAACTTATTTTTTGTGACTGGTCTGTGCTGTCTCCACCA
CAAGAACATAAGCTGCATGTGAACAGGAGCCTTGTCTATCTTGTCACCCC
AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTTGAT
GAATGAAGTGCTGGTAGTCCAACCTGTGTTTCTTGTCTGTGTAAGTATGT
CTGTTGTGGTTTTCTAAGAACCCTACAGCTCTCCCACTGTGACTCCTGTTT
TATGGTCTCTGATTGTGCTGGACTAGAATCCTAACCTACATGCTTACTCTTA
GTGTCCTCCCCAGAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGG
CTAAGACCTAGCTTCCAACCAGACAGGCCTACGCTGAGACCTCAGCACCG
CCCTTCTGCGGTCTCATCTTAAACGCATCCTTCAGGGCCCAGCTTAAATG
TCTCTTCTCAAGGAAGGCTATCCTCTTCTGCCCCCTCAGTGCTCTCCAT
GCCTCCTCTATGCCTCCATGCCTGCTTTCAACCTGCAGAAGTGGAGAAA
TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCCTTGGGCCAGGGAG
CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGTGCCCAGGTCCATGCTCA
CTTCTGAGCCCCAGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCA
GAGGAAGGACGTGCTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGA
GAGAAGGCCCAGCCATCCTCTTGCCCTCTTCTTCTCCTGCCCCGAGT
AATAAAGGTGCCTGGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACC
ACACATTCAGTTCACACCCGTCATCCACATGGCTGGCTGTGCAGGTAAA
CGCAGAGTCTGTTTACACACCCCAACCATCTAGTATTGGATGGGAGGACA
GTAGCGTGACACTCTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCA

FIG. 3 (15 of 52)

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ACCCAGATACCAGAGGAGCCCTGTACTGGGATGCTATTGGATGCTTGCC
AGTCATGTACAAAGTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATC
TTCCTCTGTAGGGAACCCAAGAGGGGAGAAGAGATATGTAGTAGGATTTA
ACCTGCAAATCCTCTGCTGAGCACCCCTGCACTACATACAGTGGGTAGCAT
GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT
GGTGACACAATCTAAGATCCCAGGGGTGGGGAGACCACACGCTTGTTAG
GGAGACCCAAAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTA
GTGACAGTGCAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTG
CTATTTTCATCATAGCACTGTGCAGGCCAACCCCTTCTGCTCCACTGGCTG
TTGGGAAAAGCTTTCTCTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTT
CCACTCTCTCACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGG
CTGCTTGTCTGCTGACTCATCCCTTGGTTTTCACTTGGAAAACCTACCACC
AGCTGGCCTCTTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGG
TGTGATCTCACCTCCACACAGTAGATTGCCTCAAGGCCAATTCCAATAT
GAATAAAAATGATTATTTTGTCTCTTCCAATCTTCTTTTAAATATTA
TTTTATAATTCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTTACCT
AAGAAATGTTAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTTA
AAATGGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG
TGGTTGGCTTTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCA
TGCTTTCCAATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGAC
CTCTGATAACCTGCCCCACCGAGTAAAGACTTAGCTGGGAAAGTCAGCT
TCATGTGAGGTAAAAGGAACAGGTAATACACAATCCCCTGCCAAGT
TCGGGTGTGCAGGCCTGAGCTTCTGCTGTGGGAGGAAAGAGAAAGAAG
AGAGAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG
ACGCAGAAAGCTGAATGGCACAGTTACCACTATTGTGCTGAGGTTCTGTG
GCCTCTGGGTCTCTTGACAACCTGGGCAAAGACCCACAGAAAATATCTCT
AGACCTACCTGTGGGAGGGGAAAGTGCTTAAGATCATTTACAGGACAGC
CACCTGGACCTCAAATGGCTTACAGTTCCTTCATCCAGAGGCTCTTCATT
TAGTACATACCAGGTGCTAAGCTGGGTGCTGGAGACATGACGGGGAACCC
ATTTACCATGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCA
AAGGGGAGGGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGC
AAGGGAGAAGCCAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAAGT
GGCCTCAGTGCCAGGTTGGACTGGAGATGGGGCTGAGGAGCTGTACAGA
GCATTCTGGACACAGATGTACATAGTCCCTTGAGGTTAGGGTCTTAGG
CATGGCAGCATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTCTGA
CAATGTGGAAGATGGGTCTTGACAGAGAAGGGCAGGGCTGTGAGACCAGT
TAGGAGACTAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGG
GGCAGGTGCAGGGCCAGAGAGAAGCAGATGGCTTCTGAGGTTTTAAGT
AGGTAGAATCAAGGCAGCTGGTACAGATCTTTTATTACATATAAACTGGA
ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGAC
AGAAATGGAATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGA
GTCCAACACTGGCTGCAATCATAAAAATGTAAACAAACAAAAATTTGCT
AGGTGTGCTTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTGTGT
TATGGCTTAAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCC
CAATGCAACAGAGTTGAGAGATGGGACCTTTAAAGGTGATTAGGTGATA
AGGGTTCTGCCCTCATAAATGAATTAATACTGTATCATGAGAGTAGATT
CCTGATAAAAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTGTGCTATG
CTTTCTGCCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCC
TCACCAAATGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAAAATGTA
AGCCAAACAAATTTCTGTTTATTATAAAATACCCAGTCTCAGGTATTCTG
TTCTAGAAACACAAAATGGACTAAGATCATTAATATCATTTTTTATCA
GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTTCTTTTCTTTT
CCTGCCTGACCTTATTACCTCCCATCCCAGAGCATCCATTTATTCCATT
GATCTTTACTGACATCTATTATCTGACCTACACAATACTAGACATTAGGA
CAATGTGGCCTGCCTCCAAGAACTCAAATAAGCCAAGTGAATCAGAGA
GGATTAATCACCTGCCAATGGGCACAAAGCAAGCTGGGAGCCAAGTC
CCAAAATGGGGCTGCTGCTTCCAGTTCCTCTCTCTGCAATTGATGTCA
GCATTATCTTCTGCTCCAGTCTGTCTCCACTACCACTTTCCCCCTCAA

FIG. 3 (16 of 52)

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CACACACACACACAACAGCTTAGATGTTTTCTCCACTGATAAGTAGGTG
ACTCAATTTGTAAGTATATAATCCAAGACCTTCTATTCCCAAGTAGAATT
TATGTGCTGCTGTGCTTTTCTACCTGGATCAAGTGATGTCTACAGAGT
AGGGCAGTAGCTTCATTTCATGAACCTATTCAACAAGCATTATTCACTGAG
AGCCTTGTATTTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTGC
ATCAAAGCCTCTAGTCTCATAGAACCTTAGTCTTCTGGAGGATATGGAAAA
CAGACAAACCCAAACCAACAAAGAGCAAGATGCTGCAAAAAAAAAAAAA
AAATGAATAGGGTGCTAAGATAGAGAAAAGTGGGAGAGTGCTATTTAGAC
AAAGTGGTAAAAACAAAGCCCTTGTGAGATGAGAGCTGCCGACAGGAGG
GGGCGGGTTCATGGTTGTGGGTTTTTGGGTAGGACATTCAAGGAGGGGGC
GGGTCTGGTTGTGGGTTTTTGGGTAGGACATTCAAGGAGGGGGCGGGT
CGTGGTTGTGGGTTTTTGGGTAGGACATTCAAGGAGGGGGCGGGTCTGTG
GTTGTGGGTTTTTGGGACATTCAAAAGAGTCTGAATGCACCCAGGCCTAC
AACTTCAAGATGGTAAAGGACAGCTCCAAGGATCAGAAGAAGCATGCTTG
GAACTGGGGCATTTTGAGAAGGAGGAAAAATATGCAGAGACTAGTGCTTG
CAGAGCTTGCATGTGGATTTTCAATTTGAGGTACAATGAAAACCCATTATG
GGTTTTACACAGTGCAATGGCCTGACCTCACTTATATTTCTTAAATAGA
AAACAGATCAGAAGGAAGGCAATAGAGAAGCAGAAAGTCCAATGAGGAGG
TTTCAAGCAGTGTGGGGTGGGGTAAGGAAAAGAGTGGAAAGAAACA
GACAGAATTGGGTTATATTTTGGAGATAGAACCAACAGAAGGAAGAGGAG
AAACAAACATTTACTGAGAAGGGAAAAAGTAGGAGAGGAATAGGTTTGGGA
AATAAATCTGCTGACATTGGAAACCCCAAGGAAGCCTCAAAAGTATATT
TACTTGTCTTAGATTTAAAAGAAATAGGAAAGAGCATCTCAACTTGAAT
TTGAAATCTATTTTCCATAAAAGTATTGTTAAATCTACTCATACTCAC
AAGAAAAGTACATTCTAAAGAGTATATTGAAAGAGTTTACTGATATACTT
AGGAATTTTGTGTATGTGTGTGTGTGTGTGTGTGTGTGTGTGTAAAC
CTTCAATTGTTGACTTAAATACTGAGATAAATGTCTATTAATGCTAAAT
TGATTTCCCAAAGGTATGATTTGTTCACTTGGAGATCAAAATGTTTAGGG
GGCTTAGAATCACTGTAGTGCTCAGATTTGATGCAAAATGTCTTAGGCCT
ATGTTGAAGGCAGGACAGAAACAATGTTTCCCTCCTACCTGCCTGGATAC
AGTAAGATACTAGTGTCACTGACAATCTTCATAACTAATTTAGATCTCTC
TCCAATCAACTAAGGAAATCAACTCTTATTAATAGACTGGGCCACACATC
TACTAGGCATGTAATAAATGCTTGTGAATGAACAAATGAATGAAGAGCC
TATAGCATCATGTTACAGCCATAGTCTTAAAGTGCTGTTTCTCATGAAGG
CCAAATGCTAAGGGATTGAGCTTCAGTCTTTTTCTAACATCTTGTCTC
TAACAGAATTTCTTCTTTTCTTCATAGGAGATGCCTGAGATACCCAAA
CCATCACAGGTAGTGAGACCAACCTCCTCTCTCTCTGGGAAACTCACGGC
ACTAAGAACTATTTACATCAGTTGCCATCCAACTTGTTTATTGCCAC
AAAGCAAGACTACTGGGTGTGCTTGGCAGGGGGGCCACCTCTATCACTG
ACTTTCAGATACTGGAAAACCAAGCGTAGGTCTGGAGTCTCACTGTCTC
ACTTGTGCAGTGTGACAGTTCAATGTACCATGTACATGAAGAAGCTAA
ATCCTTTACTGTTAGTCAATTTGCTGAGCATGTANTGAGCCTTGTAATTCT
AAATGAATGTTTACACTCTTTGTAAGAGTGGAAACCAACTAACATATAA
TGTGTATTATTTAAAGAACCCCTATATTTTGCATAGTACCAATCATTTTA
ATTATTATTCTTCATAACAATTTTAGGAGGACCAGAGCTACTGACTATGG
CTACCAAAAAGACTCTACCCATATTACAGATGGGCAAAATTAAGGCATAAG
AAAAC TAAGAAATATGCACAATAGCAGTTGAAACAAGAAGCCACAGACCT
AGGATTTTCATGATTTTCAATTTCACTGTTTGCCTTCTACTTTTAAAGTTGCT
GATGAACCTTAAATCAAATAGCATAAGTTTCTGGACCTCAGTTTTATCA
TTTTCAAAATGGAGGGAATAATACCTAAGCCTTCTGCCGCAACAGTTTT
TTATGCTAATCAGGGAGGTCAATTTGGTAAATACTTCTTGAAGCCGAGC
CTCAAGATGAAGGCAAGCACGAAATGTTATTTTAAATTATTATTATA
TATGATTTATAAATATATTTAAGATAATTATAATATACTATATTTATGG
GAACCCCTTCATCCTCTGAGTGTGACCAGGCATCTCCACAATAGCAGAC
AGTGTCTCTGGGATAAGTAAGTTTGATTTCAATTAACAGGGCATTTTG
GTCCAAGTTGTGCTTATCCCATAGCCAGGAACTCTGCATTCTAGTACTT
GGGAGACCTGTAAATCATATAAATGTACATTAATTACCTTGAGCCAGT
AATTGGTCCGATCTTTGACTCTTTTGCCATTAACTTACCTGGGCATTCT
TGTTTCATTCATTCACCTGCAATCAAGTCCTACAAGCTAAAATTAGAT
GAACTCAACTTTGACAACCATGAGACCACTGTTATCAAACTTTCTTTTC

FIG. 3 (17 of 52)

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TGGAATGTAATCAATG1. TCTTCTAGGTTCTAAAAATTGTGATCAGACLA
TAATGTTACATTATTATCAACAATAGTGTGATAGAGTGTATCAGTCA
TAACTAAATAAAGCTTGCAACAAAATTCTCTGACACATAGTTATTTCATTG
CCTTAATCATTATTTTACTGTCATGGTAATTAGGGACAAATGGTAAATGTT
TACATAAATAATTGTATTTAGTGTACTTTATAAAATCAAACCAAGATTT
TATAATTTTTCTCCTCTTTGTTAGCTGCCAGTATGCATAAATGGCATT
AGAATGATAATTTCCGGGTTCACTTAAAGCTCACATTACACATACACA
AAACATGTGTTCCCATCTTTATACAAACTCACACATACAGAGCTACATTA
AAAACAATAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCCAGCAC
TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTCAGGAGTTCAAGACCA
GCCTAGGCAACATAGTGAGATCTCATCTCTACAAAAAATGAAAAAT
TAAAAATGAGCTGGACATGGTAGTACACACCTGTAGTCCCAGCTACTCG
GGAGGCTTGAGGTGGGAGGATCACTTGAGCCTGGGAGATGGAGGCTGCAG
TGAGCCATAATCACACCATTGCACCCCAACCTGGGCAACAGAGTGAGACC
CAGTCTCAAAAGATAAAATTTTAAAAATGTTAAAAATATATAAAAGAGA
ATTTTAAAGAAACAATAATAGATCAAAGCATGGATGCAAGATATATTTA
GTTGGAAATCAAGGTTAAATCAAGGGATCTTGAATTAGGTGTGGTAG
ATTTGGGTAAGGAGTAGTCTAAGATGACCCTGTTTCTTGGTACTGGAGAC
TGGATGAGTGGCAGCGTCTTAACCATATTTTTGGTAGAAATATGGAGGTC
TTCTCCATTCCAGGATGAATGATGAGTAAATTTTAGGCATGTAATTTGA
GCTACTAGAAGGACACTCAATTGCAGATGTACAATGGGGAGATGATAACC
TATCTGGAACCTCAGAAAAATACTGTATATAGATATGAAAGACATCAGTA
GGTATGTAGTAGATAAAATCCTAAAGTGATGTCAAAGGGAGAAGAGAAG
TATATGGTGAACACTGTTGTTTGTCCATGCAATTGCCATCTCTTCTCTT
CCTTACTGACAGAACCCTGATTTCACTGAGAAGTCAACATGCCCTTCCCC
AATTGATGAATCCAATTGGTTGAAGATTATGTTCAATTCTATTCTTACATG
ACTAAGTCACGTTGACTTAATCCTATCAAATGAGATGTGATCTGGAAAC
AAGTTCTGGAAAAGATTTTCTACCTTGATAAAATAAAGAGCCATATAGAT
GGTCTTTTATCTTCTTCTTCTTGAATGAGATATGTTCTATGAGGAAGT
GAAGCTTAGAAGTGTGGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC
ACACAATGAAGAATGCAGAGTGGGAAGGAGAAAAAGAGCCAGCATCTCTGA
CAACATTGTTACACCGAGAACCCTACCTCCAGATTTTAAGAAAACAAGAAA
TGCTACTGTTATTAAGCCATTTCACTGGGTTTGCTATGACTTGCAGTCAA
ATCTAGCTTAACTGATACAGAGCACCACAGAGAACTGGTCTCTCATTTGT
CTCATCCTGTTCTTTCTAGCAGCCACGACTTCTTAGGGTTTCTTAGCC
CAAGTCTGGCTAGAGCAAGACTAAGTAAGACTTGATTCCTTAATGTCCTT
TTGTTTTAAGAAATATTAAAGAATTATTTTTATATTAATATATTTAAGA
AATAAGGAAATACAAAACACTGAGCAAGCAACACAAATCAAGAAATCTT
AAAAAGTATAATAGCTGCTCAGTCTCTGATTACAGTGAAATATGGAATC
ATTGTAGAAATGGCCTTGAGCGTTATTCTCCAGGCCAGCTATCCTTAT
GGTCTGCCCCACCTCCCTCATTGCCTAAACAGTAAGAGAGTCCCATGGTG
AGACTCAACAGTCTTAGCACAGAACTTGTTACAGTCTATTTCTTTCTTA
CAGTCTATATATCAATTCCAAATCAATGAGAGTAAAGCCCAATCCCTGC
CTTTAAACCCAAAGGACAGAAGCCCAAAGGCCAAAGATATTCCCTAACCT
TCTCCCCCT

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CCTGTGCTCCCTATGTTTAAAGCTGGGGATCTCTTTTTCTGTGTCTAA
TTATTTTCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTG
TATAAAATAGAATTAGCCAAGTGCAATGTCTTTATTCAGAAGAAATTTCA
TGGACGTTGTGCCTACTCTCTGGCTTCTGGCTTCATGGCTTTCCAGAT
CCCAAGTAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA
TAAATGAAGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGG
CCTTTAAGATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCAT
GCATATATAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA
GAAAGGAGACCCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCA
TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCA
AGAAAAGCCAGAAATCCAGGTTTTTGGGTGAAATGTCCTGATTTTAAATGT
TGGGAACATAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTT
GTATGTGGAACGCTTTCTCCAGTGGCGACCAAGTTTGGACCGTTGATAC
TCAGCAAGTTTCAAGCAAGTGCGCTTGTCAATTGTCAAGTCAAGGTGAT

FIG. 3 (18 of 52)

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BTGTGATTGGTCAAACAATTAGTTTTGCTCAGCATCTCGTGTGTTTTCA
AGGACCTGAGGGTTTCATTTGCCCATGCAGATCTTGTAGTCCTGTTTATTC
TATTAATTTATCTTGCAAATCTATAATGTTTTATTTAAGCAGCGAGAGC
CGTGGCAGCCTTTGGTCTGGACCCTTTCTAATGATCATTTAGTATCAGGC
TATGTGGGAGTTGATTGTTTTGCATTGCCTGAAAGCCAACAGTATCACTC
CTCCTCTAGGTGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG
GTGTGTATGCAGTGTGGGGGAAGCGAGGCACAGGGGACAATACTGTGGT
GTATAAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAAAATGA
TTTTTCATAACAGCACAAGACATTATTTGTTTTTGCCTCCCTCTCATTTTT
TTTTTTTTTTGAGACAGAGTCTTGCTCTGTCTCATCCATGCTCGTGTGCAGT
GGTGCAATCTCGGCTCACTGCAACCTCCACCTCCAGGGTCAAGCAATTC
TCATGCCCTCAGCCTCCTGAGTAGCTGATTACAGGTCTGCACCACCCCGCC
GGCTAGTTTTTGTATTTTTAGTAGAGATGGGGTTTTGTAATGTTGGCCAG
GCTGCCCTGTCATTTTTTTTTACTAGTGTCCAGTGGAGTTTTTTAGGGG
CTACATAACATGATACTGTCTAATCTAATGGCTAATGAAAGGGATATG
TATATGTTTTTGTGTTTAAACAAACTTCTTTGGGGTCTCAATAATTTT
TAAGAGTATAAAGGGGTCTGAGATCAAAGAGTTTGAGTCTGTCTGGACT
GGGACAGTGGTTGTCAACCCAGATTGTACATTAGGGTCACTCTGGGAAGCT
TTAAATAGTACTGATGCCCAACCTTACCGCAAACCAATTAAGCCAGAAT
CTCTGTGGATGAGAAGTCTTCATTGTCTCATCACCATGACCATCATCAT
GTCTACCGTCACTACACCATTATCATCATCATCATATCATCTTCATTATC
ATTGTTAGTATCTCCATCACCATCATCAGCATCACCATTATTATCATCAT
CATCATCCCCACCATCATCTCATCGGAACCTCACCTGCATGGAGGACAA
TCCACTATGCATTAGGTGCTATGCTATTTGCTATACTCCTTATTCTACA
ACTGCCCAGAGAGGCTGATATTATCTCACTTTATAACAGGAGGAATCTGG
ATCGGAAAAGTTAAGGTAAGCTAATTCACAGAGCGAGAAGAGATAGAGCC
AGGATTCCGAAACCAAGTCTCTGTCTACATCAATGTTCCAGTCTCTGCACT
ATTGAGAACCTCTTTAGTTATGCTTTCAACCCCTCCAACACCACAGTAAAT
TTTTCTTTTTTAAAAAAATTATACTTAAGTTATAGGGTATATGTGCA
TAATGTGCAGGTTTGTACATATGTATACATGTGCCATGTTGGTGTGCTG
CACTCATTAACTCGTCATTTACATTAGGTATATCTTCTAATGCTATCCCT
CCCCGCTCTCCCCACCCCATGACAGGCCCTGGTGTGTGATGTTCCCCACC
CTGTGTCCAAGTGTCTCATTTGTTCAAGTCCCACCTATGAGTGAGAACAT
GTGGTGTGTTGGTTTTCTGTCTTGTGATAGTTTGCTCAGAAATGATGGTTT
CCAGCTTCATCCACGTCCCTACAAAGGATATGAACCTCATCTTTTTTATG
GCTGCATAGTATTCCATGGTGTATGTGTGCCACATTTCTTAATCCAGTC
TATCATTTGCTGGACATTTGGGTTGGTTCCAAGTCTTTGCTATTGTGAATA
GTGCCACAGTGAACATTCATGTGCATGTGTCTTTATAGCAGCATGATTTA
TAATCTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTAT
TTCTAGTTCTAGATCCTTGAGGAATTGCCACACTGTCTACCACAATGGTT
GAATTAGTTTATAGCCCCACCAACAGTGTAAAAGCATTCTTATTTCTCCA
CATCTCTCCAGCACCTGTTGTTTCGTGACTTTTTAGTGATTGCCATTCT
AACTGGCACCACAGTAAATTTTATAGATTTTATAAGCAAATTTGATTTA
CTGTGCAAGAATTGGTTTATTTTTTAAACCATGTGTTGCAAACATACAAT
GGTTAATTGTGATATTTGCTCAGTACAAGATCATCAGATCACTACACAGA
CTTGAGGTAATTCACCTAAAAGCAAAGAGAACTGACCCACATTAAGT
AGAAGTCTTTACTTATTTATTCCTATAAACGAGCCAATATGAAGAGAAG
GCCTTAATGTGGTTAACTATGTAATTTTTTTCTGACTTTTGAAATACTG
AGAAGAGCTCATGACTCTCCCATCTCCTAATTTCTACCTTGGTGGATTTTA
GACTGACCACAACTCATGGGTAAATGAGGGAAGACGAATAAGAAACCTTG
CTTTTTTTCTCCTTGTTTTTGGCTGGCTGCAGTGGCTCACACCTGTAA
TCTCATCACTTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT
TCAAAACTGGCTGGGCAACATAGTGAGACCCCATCTCAAAAAAAAAA
AAAAAAAAAAAAAGGCGACAGGCGGTGCGTGCCTGTAATCCTACCTACTC
AAGAAGCCGAGGTGGAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG
TGAACCTTGATTGCACCACCTTATTCCAGCCTGGGTGACAAAGCAGGACG
CTGCCCTCAAGAAAACAAAAACAAACCTTAATTTTTTGGCTATTCTTTTC
TGGTAAGAAATGGTATAGAGATGGGGATGAGGATGGCTATTGTATGAGAGA
GCAACAGGGTCCAAGCAGTGTCTGGGCTGTCTAAGGACCAGTAGTCAG
CTTAACCTCTCAAATTTCCAGGGAAGGAGTTCGAGTGGTAGAATATCCT

FIG. 3 (19 of 52)

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GGGTATGCCCAAAGCATCACCTTGCAAATAGCCTGTGATGAATAATTTG
 TTCATTTGTTATGACTGGAACTGGCTTTGTGTATGCCAGAGAATGGGGG
 CAGGAAAGAGAGATTGGTGTCTTGAGCTCTCTGTGCCTCTGGGGCAGTGA
 TGCTTTTCTCTCATGTGGAAGGAGAGCATGACTGAAAAGGTGCACAAAT
 AAGGTGTCTGTGAGAGAAATTAACCTTCCAGATACAGAGACACAACCTTC
 CCCAAGAGGTCCTCATTGCTCTGCCTTTTTTCTTTTTTTGCTTGTTC
 AQCATTATAACAGAACTGATTATGACCTCAAAGAGAGGAGAAAGCGA
 CTCTCCCCACCCTAGAGCTAGTTAACCACCATATCTTCTAGATATCCTT
 GAGAGCAATGTAACCC

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GTGAACCTCGTTTTACCTGTGTAGCAGACCAAGCCGACAGACAAAATCCNTC
 AGACACCAAATTAAGAAGGAAGGGCTTTATTGGGCCTGGAGCTGCGGCA
 AGACTCACGTCTCCAACAACCGAGCTCCCCGAGTGTGCAATTCCTGTCCC
 TTTAAGGGCTCACAACTCTAAGGCGGTCCACATGAGAGAGTCGTGATAG
 ATTGAGCAAGCAGGGGGTATGTGACTGGGGGCTGCATGCACCTGTAGTTA
 GAATGGAAACAGAACATGACAGGGATCTTCACAGTGCTTTTCTATGCAAA
 TAACCGATTAGATCAGGGGTGATCTTTACCAGGCCAGGGTGTGTACC
 GGGCTGTCTGCTTGTGGATTTCAATTTCTGCCTTTTAGTTATTACTTCTTT
 CTTTGGAGGCAGAAATGGGCATAAGACAATATGAGGGGTGGTCTCCTCT
 CTTACCTGCGGGGAGTGAGCTCAAACCTCTTAAAGGAGTTACCTGCCTTC
 CATCATCAGGGAAGCAGGAAATCTTGCCTTCCTTGTGGAAGCAAGTAAA
 ACTCAAAACAAACAAAGAAAAAACAGGGAGTTGTACAGCAAAATAAAT
 TTTGATTTTGACCAAATTTTGGGAGATCAGGAATCTCTGAAGGAGATGC
 TTTGAGACCTCAGCAAATTTCTCTGTTGGTTTGGCCATAAAGTTAGCTC
 ATGCTGGTACCAAACACCACTAGGAGATTTGTCAAAGGTAAGAGGCATCT
 CCACTCAGAATCCCTTCGTGGTTACCAACATGTGAACCTTGGAAATCTGA
 GACAGGTCTCAGTTAATTTAGAAAGTTTATTTTGGCCACGGTTGAGGACAC
 CCACCATGACAGAGCATCAGGAGGTCTGACCACATGTGCTCAGGGTGG
 TCTGAGCACAGCTTGGTTTTACACATTTTAGGGAGACATGAGACATCAGT
 GAATATATGTAAGATGTACACTGGTTCCCTCCAGAAAGGCAGAACAACTT
 GAAGCAGGGAGGGAGCTTCCAGGTCACAGGTAGGTGAGAGACAAACAATT
 GCATTTCTCTGAGTGTCTGATTAGCCTTTCAAAGGAGGCAATCAGATAT
 GCATTTATCACAGTGAGCAGAGGGGTGACTTTGAATAGAATGGGAGGCAG
 GTTTGCCCTAAGCAGTTCCCAGCTTGACTTTTCCCTTTAGCTTAGTGATT
 TGGAGGCCCAAGATTTATTTTCTTCTACATCACTGTGGGCAGCTGACT
 AGGAAAGCTTTGTAGGACTGGTGGGCAGTGTGAGAGCCAGTGGGGGGTG
 GTGGTCTGTGCCAATGGTAGCAACCCTGTGAGGCTGAGTAACTCAT
 TTCCCAACCTCCTCTAGCAGCCCCAGTGGAGATACAGAGGAAGCAGACTA
 GCGATACAACCCAGCCTGAAGTTTTGTCTGGTGAGTGTAAATGGAATAAAA
 ATGGGAAGGGTGTGAGAGACCCAGCAAGAAAATGGTTGAAGAGATGGGG
 CACAGAAATTAAGCTGGATCAAAAAGGACGGAAAAGCAGAAAGGGCCGAT
 AGAGAGAGGGGATATCTATGGGTTCCGCGATTCTGAAAAGGACAAATCACT
 GGTGCTTTGAGAAGAGAGAGGGGTGAGAAAGCAGGAAGGCTGGAGGCTGTC
 ATCCAAGAGGCGGACATCTGTGAACATGATTCCAAGAGTACCAGACCAT
 GGGGGTGGCCAAAGGGAGTGCCTCTTCTCACTCTCTACTCTTAATTCCTT
 GTACTCAAGATAATAAGTTCCAGAAAGAGAAGTACCCATATTTAATTCAT
 CTGTGCTCTTCTAGCAGTACTAAAAATATTTATATGAAAGGTATCAAACCT
 TTGAGAATGTGTGCTGCTAAATTTGTTAAGGATGCTGGAAAACCTCAAGACG
 TCCCTGATCCTGAGCCTGAGTATGAGCCTGTGGTGAGCCCAATGCAGGTC
 TCCATTGAGACAAAGGCTCAGGGAACGGATGAGACCTAGGGACAGAGAT
 GCATGCTGGAGCAGCATTCCCCATCCCTACTGCAGCTCAGGCCAGCTGAC
 TGCTTTATGAGTAAACGTTACCAGGGAACACTTTGCAGTCTTAACACACA
 TGCCACCTGTGACCACTGATCCCTGTTGGGTGACCACTGACATCAGAGA
 TTCCGATGGCAGCAATGAAGACAAGGCTATCCTCATTAGGAAGGAAAGGAA
 GGAGGAGGGAGGAGGGCAACGAATCTTTCTGCTTGTCAACCACGTCCA
 TCTCTGTTAGTGATTTCCTATGTGTGACTTTGTTTATCTTTATAATAAC
 TCTGAGAGGTAGTCTTGATGTCCACATTTTGAACATGAGGACATCCAGC
 CAGGAAGTTGAGTTCTGGGGACATAGCTGAGAGGGCAAAGCTACATATAA
 ACCCTCTTTGTTTTTCTGGCTTATCCACTGAGTGCCCCCTGCAATCCA
 CCAGCCCCATTTGTGAAGTGCACTATAGGTAAGTTGGCACAGGAGGAGT

FIG. 3 (20 of 52)

GGATGTGGGGCGATTGTTGACAGCTCTCCAGGAACTTACACACTGGTGAG
GAGGGCCAGGTATGTTCTGACCAGTCACAATCAAAGCAACCTCCTACTA
ATCAGGGGAGGCTTGGTACCTGGGGAATGCTATGTTGAAAGGTTCTTTCT
GGGTTTTAAATGATGGGTCTATTTCTTATTCTTAAGATTGCTTTTTTT
CTGGCTAGAACTTAAAAGAAAATTTTCAGTAAAATTTCCCTTCCCTGGCAC
AAAGTGAGCTTGAAATGAATTTCCAGGTGGCCTTGATACTTTAAATATT
GCCTCCTATAAAATCAACCTTTAGAAGAAGGAAGTCAAAGAACATGCTAG
ATTTCAAAAGGTTAAATTCCTTGAAATCCAGTTATCTACAGGACAATGTT
GTCAAAGAAAAAATTTATTTGGCCAGGCACGGCGGCTCATGCCTATAATCC
CAGCACTTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTGAGGAGTTCGA
GACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAA
AAATTAGCCAGGTGTGGTGGTGGGCACCTGTAATCCAGCTACACGGGA
GGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGAGGAAGTTCAGTGAG
CCAAGTTCAAGCCACTGCACCCAGCCTGGGCAACAGAGCAAGACTTTGT
CTCCAAAAAATAAATTTCAATGATATTTTTAAATTCATGGTAAGGAA
GATTTCAATCAGAACCAGCACAGAAGATATAGGAAACACTGCAATGGGAC
TTTGCGGTGGGGGAGAGAGATTGAACACAACATACATATACAGCACGGGCA
AGGACATATTCATAGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT
TACTAAGAGGAAACATGAAAAATAAGGGAGCTTCTGCCTAAACCCACCTA
ACCGGATCCTTGCTGAAGACAGGACAGGGTGATTGGACACCCTTTGGGG
ATGGTGGAGGATGGGGAATCCAGTGAGATTTCAAGGGTGATGCGATATTG
AACATACAAAGTTCTTGCTAAAAAAGGATTTTACAAGAAAGTGACAAAT
GTGCCTGGGACAAGGTGCAGGAGCCCGACGGAGATGTGGTCCAGCAGAGA
ATATGTGCCGAGATGATAGGTGAGTTCTCTGACGAAGGATATATGCTGAT
CCAGCCAGGGTGAAATGCTCAGAGAAAGCACGGAGGGGCTATGTCCGTTG
CCCCAGTCTCCACGCGGTCAAATCTGATCCCGTTGTGAGTGTGGCCGTTT
GTAGAAAGCAATCAGGGGGGGTCCCTCCCC

>Cont:g30

AAATATATTTTTTATANNAATNTGAGACAGGTTCTCACTAGGTTGCCCAG
GCTGGTCTTGAATTCCTGCCTTCAAGTGACTCTCCACCTTAGCCTACTG
CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAATTTGCTTC
TCATTCAGCACTTTTTATTCCTGATTATATGTATATGTATATCTGCA
TCATCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATATATAT
ATGGAATATCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATAT
CAGTCT
CAACGAGTGTGATGTTGTGAAATATATATTTGTTCTTCTCTCTCTCTCT
CTGACATACAGCTTTTAAAAACCCCTTGAATCTCTGGAATAATAAGAGTG
TCTTTTGCATGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG
CTTCATGATGGGGTTTGTACAGGAAAGACCAAGGCAGGATTGGAGACTT
GAGACTGTTAGCCCCCACTCCCAACCACTGGAGGGAGTGGAGGGGCTGAA
GGTTGTGTGATCAGTCACCAATGGCCAATGGTTCCGTCAATCATGTGTATGTA
ATAAAGCCACTCTTAAAAACCCAAAAAGGACAGGGTTTGAAGGGCTCCC
AGATAGCTGGACACATGAAGGTTCTTGGAGGGTGGTGGCCCCAGAGGGGCA
TGGAAGCTCCACACCCCTTCTCATATGCTTTGCTCTGCGCATCTCTTCAT
CTGGTGTTCATCTGTATCCTTTGTAATATCTTTAGAATAAACTGGTAAA
CTTAAGTGTTTTCTGAGTTCTGTGAGCTGCTTAGCAAATTCACGGAAC
CCGAGGGAAGCAAACCCAGATTTATAGCCATCAGTCAGAAGCATAGGTGA
CAACCTACCACTTTGTAACCTGGCACCTGAAGTGGGAGGCAGTCTTGTGAGA
CTGAGCCCTCAACCTGTGGGATCTAACGCTAATCCAGGTAGATAGTGTT
GGAGTGAAATAGGACACCCCACTGGTGTGCGCTGCTGGAGGACTAGTGGT
GGGAGAAATCCCCAAGCATTTCCGTGACTAGAGGTACAGAAGAACTCAG
TGTTGAGGTGTTGTGACAGTATGGTAGGGAATACTGCGTCTGGTTTTTTC
CTTTTACAATCAGTTAAATATTTTAAACACAAGTCTACTGTATATTAGTAAA
AGGGTTACATTTTTTAAATGTCTTGACAGTTGCACTTTGACAACTTCCATA
TCAATCACTTTTTTTCGTGTCCGTTTGAACCAAATCACTTGGGATACC
ATGAACCAGGCTGCAGCGTATTTCCCAAGGCCTTGAAGCTTGGAGGCCAT
TTTGCCAGCCNTAATCCCTGTGAATACCAGGCTTCTGAGTTTAAAAAT
AGACTTGAGGCCAGGCCTGGTGGCTCACACCTGTAAGCCAGCACTTTGG
GAGGCAGAGCGGATAGATCACAAGGTTAGGAGTTCAGAGCCAGCGTGGC
CAACATGGTGAAACCCCGTCTCTACTAAATATACAAAAAATAATAGCCG

FIG. 3 (21 of 52)

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GGCGTGATGTTACAGCAGTAGTAGTGCCAGATACTCAGGAGGCTGAGGLAG
GAGAAATACCTTGAACCTGGGAGGCAGAGGTTGAAATGAGTCAAGATCGTG
CCACTGCACTCCAGCTTGGGCGACAGAGTGAGACTCAGTTTTTCAGGGGAG
TTAAAACAATACAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG
ATGGATTTAGGGGAATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA
CTCCACCTGTCCAGAAATTGGACCTCACCAGGGGAGGTCTGTGGGGACAGG
GAGAGGCCCTCTGCCTCCACCCCTCCTCTACTCCCCAACCCCTGAGTCA
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTGAGTTTGGCAATAGGTA
TCTGAAGGACTCCAGGTGCTTCTCCCTTGATTCAAAATTTTACTTATAAA
AAAAATTATAAGAAAATTCTACTTAAAAGAAATAATCAGGGAGGTACAAC
AAATTGTACTTTTTTTTTTTTTTTTTTTTTTTTGAATGGAGTCTCACTG
TTGCCCATGTGGAGTACAGTAGTGTGATCTCGGCTCACTGCAACCTCCG
CCTCCTAGGTTCAAGTGATTTTCTACTTCAGCCTCCCAAGTAGCTGCGA
TTACAGGTGTGTGCCACCACACCCGGCTAATTTTGTATTTTGGTAGAG
ACGGGGTTTCAACATGTTAACCAAGATGGTCTCGAACTCTGACCTCAGG
TGACCCACCTGCCTCAGACTCCCAAAGTGTGGGATTACAGGGGTGAGCC
ACTAAGCCCAGCCATTGTACATATTTTGTGGGTATTTACTAAAAATTAT
TCAAAATAGTAAAAAAATTGAAATAAACTGGGGACTGGTTAAATAATT
TTGGGTACAACCAATGGAATACTATACAGCCATTAAAAATTACATT
GAGGCCAGGTGTGGTGGCTCATGCTTGTAACTTAGCACTTTGGGAGGCC
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTCAAGACCAGCTTGGGCAAT
GTGGCAAAACCCCTGTCTCTAAAAAATAACAAAAAATTAAAAAGCT
GGGTGTGGAGGCACACACTCTAGTCCAGCTACTCAAGGGCTAAGGTG
GGAAGATCACTTGAACCGGGGAGGTCAAGGCTGCAGTGACCCAAAATCGG
GTCAATTGCACTCCAGCCTGGGCAACAAAGCAAGACCTGTCTCAAAAAA
AAAAAATACATTGAAGAATATCTTACGGTATGGATAAATATTCATTTTA
CAGTGATAGATGCAAAATAAAGCAAATTACAAAATATACAGTTTAATTCC
AACTTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG
TATATGTAAATATAACAATATATGTTCTATATATGGATATTATATATTTA
CACATACATACACATATATAATATCTTCTCTAGAGAGCAGAAAGAGAG
TAGACAGATAAATGAAGATAGGATACAACTCCAGTCCAGCTCAACCTAGGG
GACTTGTTTTAAAGCCTCAGGAGAGAGAAGTTGGGACTAGAAAGCAAGGC
AGCTATTTGTAAAGCATCTTTGTGTTTCATGCTATTGGGGTGGGAAACAAC
AGCACAACCTTTTGAAGCCCTTTCTACTCACCCCAAACTGCAGAGCA
GCTTTAGGACCCTCAGAGTTCAAGAAGACCATTTCAGAGTAGAAGAAGT
AAAAACATGTATGAACCTGACCTGAGCTCATGGACTGTGCCATGAGGGA
AATTCCTAAAAACAGCAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT
CAGCAAGTCCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTCTGGC
TGGTGAGGTCTAAAGACGTTTGGTCTCAATATTAAGTCTCGTGAGAGAGG
TCACAAACCCAGTCCCTTGGCCACAAAAGGAAATAAATTCTGGCTTGAGA
CATTAGGGAGGAACAGGGCAAGGGGAGGTTCAAGAAAGTTTTAATGGATG
AGATGATATTTAAGCAAGGCCCTGGAAAATGAGAAATTTCAACCAATAGCC
ATATGGTAGGTAGAGCAAGCAAGATAAGGAGGGGGCAAGTGCAAGGGGCA
ACATCAGATATGACCAGGGTGTCTGGGGCATGGCTGATGGAGAAGAAGA
TTAGACTGGAGTTTGGGAATGCCACAGTATCGAGGTTGGATTTAATCCTA
TGGGTAATAAAGCCAACTGTTCAACCCCAACCCACTTGCAATATGGCTC
CAAAATAGCAGGTGTTTGATAAAATGACTACTTTTACTCTACTATTCCCT
CCCTCTTAAGAAGAAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT
GTCCCAATCACACTATGATTTGGCCACAAAACAGAACGAAATGTTACAC
CCAAAAATGCTGCCTCCACCTCCCTTCTTGCTTCTCCTCCCTGCTGGACT
ACAGACTATCTCAAGAGTGACGTACACCATCAGGGCTTCAGCTTTTCCCC
GAAACAATGCCAAAATATTAGCCATACGTCACTGTAGTAAGAGCCCTGAA
TTGGGAATCCCAGCTTTGACGCAGACATGCTGATTGACTCTGTGACCATT
CTCTTCACCTTCTCCACTCTATTCTTCCCCACCTGTAAAGTGAGGTCCTTT
CCAGTTATAAAAAACAGATGATGCTATTGTCCTGTTTGTATCTAATCTTG
CTGTGTTATAAAAAAATAAGGCTCTGTACATTCTCTTGGCCAATTC
CCTTCTTATCTCTACTTCCACAGCCCTTTTCTACAGAAAACAGCAT
TGTCTCTTGGATCCATCTCTTAAGAAAGCGCTTTGCCTCCCCGTTATT
TAGGTGATAAGAAAGTGTCTTAGATGACAGCCCTGGAATGGGCTGGAGGCA
ACAAAAAGCAAGTGAATAGACAGTTACAGCGACGACAATAATAACAAC

FIG. 3 (22 of 52)

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CAACACCTCTCACTAAAGAGAAAGAAATAAAAAAGAAAATTAAAAATCTGC
CGCAATGCCACACAGTCATTGAATAACTGCATGTGTACAGCACTTGGTT
ACTTTTACATACTTCATATTTTAGCCTTCATAGCAGCTCACAGGGGTGGA
TTTAATTTTGTAGTCCAACCTCCTGTCACGGTGCCTGGCACAAGTATAATAA
ATGTTCTGTGAATAAATGACCCTCTTTTATAGATGAGGAAATCGAGGCTCA
AGGAGAACAAGCAATGTAATGTCCCCCTCCTGTTGAGCCATCTGCCTTTC
ACGCCACTGAATGCAGTAGTCCTCAGTGCCCTGAACCTTGACCCTCTTCTG
CTTTTCGGACTGGTCTCTTCTAATCCCGTTGTGACTCACTACACCACCTCT
CCTGCATATGACATCTACATTTTAAAAACAAACCGTATGGAAATAACACAT
TAGTCGGCTTGTTCCTCCACCCCGCAAAAAAAGGCCTCTTTATAACA
GAAACTTCTCAGGCTGGTAGGGGAATTTATTCCCCCATTTATGGTAGAA
AGGCCCTAACCTTGACCTCACGCCATAGCTATTACATGGGGGAATGAT
GAATAACATGGGGAGCAGCATGTAAATATCATTGAGCCGTAGTCCAGACC
TATAACACATC
>Contig31
GGGGGAGCTGCATGTGCCTGTGCGAGATCTGGGGGAGGAACAGGAAGATCA
AGAGTTCTGTGTAGGACATGTTAAGTTGAAGGTGCTTACAGGATAGCCAG
ATGAAGCATCAGGTGTGCAGTCAAAGATATGAGTCTGGAGCAGCACATCC
TAAGTCACCTCCTGCACCAACACAGAACTTCCAGGCCACTCACTTGAGCT
CTCCCAAATAGTTTCCAAGTGTCTATTATGTTAATAACCTATGAGCTTGAA
CACCAGATTCAAACCCCACTGCATGGCTTTTAAAGACCATCTCAAGGGCT
TGACACTCCAGGGAGCCAACTAAAGATGCCTGGTCTTACCATCAACCTCC
ACCCCAATTTTATAGAAAATGTTTCTACCTGTCTTAAGGCAGGGTCTCTG
CCCCACTCCAGGCCCTTTAGATCCCCAATATTCTCTCTCCCTGAACCA
AAACCTTCATCATCTTCCAGCATGGGTGGGGCTCCATTCTTGCTTCTGC
TCCCCCTGAGCAGAAGCAAGTTTCTCCCAACTTGACCTGATTCTCTCTCTA
AGTACCAGTCAGTCTGTTTCTGGAATGAGAGAAAAAGACAGAGTGAG
AGAGACAATCCAGAACTCTTGCTCACTCACAGCTAGGCTGGGCATCTGGG
AGGATGGCTGTGTCCATGGGAACCTGGGAAAAGCCACACCCTTGGCAGCC
TGGTCACCCACCTGTCTCCCTGGCAGATTCCGCACTGCTCTCTTGACCC
TCTACCAGGGCTAACCGGCCTGCTCACTCTCCCCAGCATGTCTTCCCAGC
CCCCTCTCTAATTATTACATTTCCCTTACATAAACTGCCCTTCTCTCCC
AATCACCACATGTTCACTTCCCACCCAGCTGTCAAAGTCTGGCTCAACCT
CATTCTTGAAAAGGAAAAAACAACAAACAAACAAACAAACAAAGCAAAAA
ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC
TCTAACTCTCACAACAACCTACAGCAGGTAGGTGTTATCACACCCATCTCT
CAGGTGAGAAAACAGGCTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG
ACAAAGCTTAAATTCAAGCCCAAGCCTGTTGGCAACCAACGTCTGTACCC
TTGATAGCTACCTCATTACCACCAATCCAGTGGCCTCAGGCCCTGGCTG
CACACTGGGATCACCTGGTGCCCGAGACCACATCTTAGACCAGTCATACAG
AATCTCTTGGGCTGGGATCCTCCACGGTACATTTTAAGGGTCCCAGGTG
AGTTCCACCATGGACCCAGAATTGAGGACCCAATACCGTATACCATCTCC
TTCTTCATCTCTTCTAAGGCATCTCTTACTCGCTGTGCACTCCCATACCA
CTTTGTTCAATCATCCAATCATTCACTTCACTGAGTCAGTTAGTCAGGAGC
TACTCACTAGTCCCCTGCCAGGTCTAGTCATGACATAGGGCTCTGGGGA
CCAACAAGAAGCAGGACCCATGCCTCCTGCTCTCATGGAGCTTGCTCTGC
AGCAGAGGAAGCAGTCAGTGAGATGTAGCAAATGTGAAATGTGCACAGAT
GGGAAAAGCAAACTTTAAAACCTTTTAGGACAAAATACACAAGAAATCTT
TGCAACTTTGGGACAGGAAGGAACAACATTCCTTACACATGACACCAAG
GAATCAACCATAAATAAAAAGGTGATCAATTTGACCTCATTTAAGTGTTA
AGCTTTTTTTCATTGAGAGACACCATTAAAAATTAAAAATACATGCCACAA
ACTGGGATACAATATTTTACAACACTTATGTCTCACAAGGATTAGTTTTTC
AGAATATATAAAGAACTCCCGGCCGGGTATGGCCGCGCACGCTGGAATCT
CAGCACTTTGGGAGGCCAGCGGATCACATGAGGTGAGGAGTTCAAGACCA
GCCTGGCCAACATGGCAAACTCCGTCTCTACTAAAAATACAAAAATTAG
CCAGGCATGGTGGCGGGCGCCTGTAATCCCAGCTACTCAGGAACTGAGG
CAGGAGAATCACTTGAGCCCAGAAAACAGAAGTTGCAGTGAGCTGAGCTC
ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAAA
CAAAAAACAAAACTCTACAAATAAATAAGAAAAAATAGCCAGCAGGA
AAAAGTATATACATTTTATAAAGAATAAATACATTCTGTCAGTTTTCTA

FIG. 3 (23 of 52)

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ACATATATTTTTTAAGAGTAAATACAAATGGTTAGGAAACATTTTTTAA
ATGCCCAACCTCATTAAAAATTATAGAAGTGAAAATTAAGCCACAATAAG
ATACGATTTTATACCAAATACAGTGTCAACACTTTGCAAGTCTGACCTCA
CCAAGTGTACCAGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG
TGGGTCTGTAAATCTGTACTACAAACAATTGCAATAAAATGTAATAAATA
TACAAATAGGTGGAGCAGGAAGTGACCTGCAACCATATAGCAGATAGGGCA
GGAAAAAGCCTATGAAAAGCTGACATCAAAGGGATAAGTTCAGTTACCCA
GCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA
TTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGAGAACCCTGAA
ATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACTATTGGGGGT
TTAAGCAGGGATATAATATTCAATTCAAGCATGCAGTAAAGGTCACTGG
CACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGTCTGTTTTGG
AAATATCACCTGGCTGTGAGATGAAGAACAGGTAGGAGGGTCACAAAAC
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTGTGTGGACTGTG
GCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAAGGCATGTGG
GAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGGGTAGAGTG
GTGAGTGAGAAGACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT
GGTAAGACATTCACTGGACTAGGATCGAGGAANGAGGTGGGGAATGGGACC
ATACCTGCAGTTTATAAGGGGTGGACGAGGGAAGATTATGCGGGAGACTG
AGAGAGGAATAGACAAAGGAATCCCGGTGCAGTATTACAGAACTGGGGT
GGGAGGGGGTGTANTTCAAAAAGGAAAGAAAATTGTCAAATAGTATGAA
ATGCTGCAGAGAAACTCACGGATTTTTTTTTTAAGCTTAGAATTATTCAT
TGACTATGTGAATAAGAATAACTTTTATGAAAGAAGTTTGTCTAAGTAG
TAGGAAGAAGCAAAATTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT
GAAGGCACTCTTTCAAGAGAAACAAAGCAGAAGGTGAGGAGAATACTAAT
GAAGGAGTTACGGCCTTCACTATTTTGTCTTTAGATAAGCAAGACT
TGAGTGGGTCTGGTGAGGAGAAACAAGTAGAGTACAAAGTTAAAGGAGAG
ACAGACAGAGATAGAGATAGGGACAGAGAGAGAGACAGAGACAGAGCACA
AAAGAGCAAGGTCCCTGAGAAACACGGGCTTCTGTTTAAACCCAGCCAG
ATGTATTGCAATTCAATTCCAGTACTAACCACCCAGAGTTGTGTAGACT
CTACAAGTTAAAGAGCATGGTCCCAACAAGACTGCTTCTACGTGAGATG
CCAGGCACACTTCAGGGGTCCCAAGCCACTCATGTTTTTTGAATGACTG
CCATAAGTTCAAAAATTCCCAAACTCTCTCAGATTCAATAACTGGGTAT
AACCCTCATAGAAGTCAAGAAAATGCTATCATTATTATTACAATTTTAT
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG
AGAGGACTAGTAAAAAACAGAGCTTCTGCGTCTACCTTCAAGGAATCAG
GATGCACACCCCTCCAGCACATCAAGTGCTCATCAACCAGGAAGTTCT
CTGAGCTCCAATGTCCAGAGATTTAGGGAGGATTCATTACATAGGTATC
ATTGATTAAATCATTGGCCATGTACTTGAAGTCAATCTCCAGTGTCCCTC
TTCTCCCTAGAGGTCTGAAGGGTTGGCTAATATCATGTGGCTCAAAGCCC
CAACTCTAATTACCTTTTTTGGTCTTTTCAGGGACTAGACCCCATCTGAA
GCTATCTACAGGCCCTGCCATGAGTTAGCTCATTAAACATAACAAAGACAC
TTATATTACTCAGAAAATTCCAACAGTTTGAAGCTCCATGTGAGGAAC
CTGGGACATAGATCAAATTCTTTTTTTTTTTTTTTTTTGGAGACAGGGT
CTTGCTGTGTGCCCAGGCTAGAGTGCAAGGACAGATCACAGCTCAATGC
AGCTTCAACTTCCAGGCTTAAGTGACCTTTCCACCTTAACCTTCCAAGT
ATCTGGGACCACAGAAAATGGCTAATTATCCTGGCTGATTTTTAACTTT
TTTTTTTTGTAGGGATGGGATCGCCCTGTGTTGCCAAGGTTGGTCTCAA
CTCCTGGGTTCAAGCAATCATTCTGCCCTGGCCTCTGTGATGGTTAATAC
TGAGTGTCAACTTGATTGGATTGAAGGATACAAAGTATTATTTTTGGGTG
TGTCTGTGAGGGTGTGCCAAAGGAGATTACATTTGAGTCAGTGGACTGG
GAAAGTCCACCCTTTCCAGTGGACTGGGAGACCCACCCTCAATCCAGGT
AAACACAATCTAATCAGCTGCCAGTGTGGTCAGAATAAAAGGAGGCAGAA
GAACAGGGAAACACTAGACTGGCTTAGTCTTCCAGCCTACATCTTTCTCT
CATGCTGAATGCTTCTACCTCGAACATCAGCCTCCAAGTTCTTCAGTT
TTTGGACTCTTGGACCTTCAACCACAGATTGAAGACTGCAGTGTGGCTT
CCCTGTTTTTGGGTTTTGGGACTCAGACTGGCTTCTTGCTCCTCAGCT
TGCAGATGGCCAATTGTGGGACTTTAACTTGTGATCATGTGAGTCAATAT
TCCTTAATAAACTCAGATATATATATATGTATCAGACATATATATATC
CTATTGTATATTATACAGATATATAATATCCTATTATATACAGATATA

FIG. 3 (24 of 52)

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TAATATCCTATTATATACAGGTATATATATATATATGTATCATATATA
TATCCTATTGGTTCTATCCCTCTTGAGAATCCTGACTAATACAGCCTCCC
AAAATGCTGAGATTACAGGAGTGAGCCACAGCCACCATGCCAGCCCCAA
ATTCTTAATTATACAACAATGGGTCCAGAGATCAGGGCCTGGGTAGGATG
CAGCAATAAGAAAACAGATGGTGGATGGGGACACATGTTGGAAGTGTC
AGGACATGGCTGAGGGAACCTCATAGGATGGTGTCTATTTTCATGGCTGAG
TGTGAGGAACAGCATAAGGTCAAAATTTAGGTCAATGGTGAGTTTTTTA
AATTGTTGCTGTGAACCCCAAAATCTGACCCAGGTCTCAGTTAATTTAG
AAAGTCTATTTTCCAAGGTTGAGAACACCCACCCACTCACGACAAGAGC
ATCAGGAGTTCTGACCACATGTGCCCAAGGTGGTAAGAGCACAGCTTGG
TTTTATATATTTTAGGGAGACGTAAGTCATCAATCAATATATGTAAGATG
TACACTGGTTCTGCCTAGAAAGGCAGGACAACCTTGAAGCAGGGAGGGGGC
TTCCATGTACAGGTAGGTGAGAGACAAACAGTTGCATTCTTTGAGTTTC
TGATTATCCTTTCCAAAGGAGGCAATCAGATGTGCAATTATCTCAGTGAG
CAGAGGGATGACTTTGAATAGAAAGACAGGCAGGTTTGCCTAAGAAGTT
CCCAGCTTGCATTTTCTTTAGCTTTGTGATTGGAGGCGCCAAGATT
ATTTTCTTTTACATTTCCCCCTTTCTTTTAAAGAACTTTTAAAGAA
AGCTTTTAAAGAAATGAGTCTCTGGTCCCAGGTTTCATCTGAATTCT
CGAGGGGAGGATGGTTTATCCTAAACGGGTGGTTCTGAATTTGAGAAAG
TGCATTGTAC
>Contig32
AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAACAAGAAGA
TGAGGGAAAGTTTGAACCTTCTAGAGACTGGCTAAATGGTTGTGACCAA
AATGCTGATAGTATACGGACAATGAAGTCCAGGGTGACAAAGTCTCAGA
TGGAAATGGGGAATTTGTTGGGAACTGGGCAAAGGTCACCTTGCTATGA
CTCAGCAAAGAAATTTGGGTGCATTGTGTTTCATGTCTGGGGATCTGTGGA
AGTTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGGAAAGAA
CCTCTAAGCAACAAAGTGTGTTGCTTAGAAATTTCTTTCTTTCTTTTTT
TTTTTTTTTGAGCTGGAGTTTTGCTGTGTGCGCCAGGCTGGAGCGCAGTG
GCGCAATCTTGGCTCACTTCAAGCTCTGTCTCTGGGTTTCATGCCATTCT
CTGCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGCTGCCACCATAC
CTGGCTAATTTTTTAGTATTTTAGTAGAGACGAGGTTTACCATGTTAGC
CAAGATGGTCTCAATCTTCTGACCTCGTGATCCACCCGCCTTGGCCTCCC
AAAATGCTGGGGTTACAAGCATGAGCCACCCCGCTGGCCTGCTTAGAAA
TTTCTAAGCCAGGATATGGCCTGTCTGCTTCTAACAGCCTGTGCTCAGGG
GTAAAGAAATGACTTAAAGTTGGAACCTATGTTTAAATGGAAGTAGAGT
CTAAAAATTTGAAAATTTGCAGCCTGGCCTTGTGGCAGAGAAAGAATCC
AAGTAGGCTGCAGAGCAATCATTGCTAGAGAGATTAGCATGACTAAAAGG
GAGCCAGTGCTAATATTCAAGACAATGTTAAAAAGGCCTTGAGGGCATT
TCAGAGATCTATGAAGCAGCCCCCTCCCATCAGGTGCAGAGGTTTGGTG
CACTAGGCCCAGAGGTTTTATGGGCCANNGCCAGGGCCACACTGCTATGC
ACAGCTTTGGGACACTGCTGCCCCGATCCAGGCCACTCTGCTCTGGCTCC
ACCTTTGGCTCAAACGGGCCAAGATAGAGCTTGGACCACTGCTCCCGAGG
GCACAAGCCATAAGCCTTGGTGGTTTCCATGTGGTGTAAAGCCTGCAGGT
GCCCAGAATGCAAGATTGAGGGAGCTTGGGCACTTCCACCTAAATTTAG
AGGATGTGTGAGAAACCTAGGTTCCCAGGCAGAAAGCATGATACAGGGGC
AGAGCCCTTGACAGAGAACCTCTACTAGGGCAATGCCAAAGGAAAATGTGG
GGTTGGAGTCTCACACATGGTCCCCACTGGGGCACTACCTGGTGATACT
GTGGGAATGGGGCTGCTGCCCTCCAGACCCCAAGATGGTAGATGCACTGG
CAGCTGGCACCTGAGCCTGGAAAAGCTGCAGGCACTCACTCCAACCCA
TGAGATCAGCCACATGGGCTACTCCAGGGAAGCCACAGAGGCAGGGCT
GTCTAAGCCCTTGGGAGCCTACCCCTTGAACCAGCTTGCAGGACATGGAA
TCAAAGATTATGTTGCAGCTTAAAGGCTTAATGTTTTCCCTGTCAATTC
AGGCTTGTGTGGGACCTGTTGCTTTTTTTTTTTTTTTTTTTTTTTTGGT
CACAGGTGTTTTGAACCAGAACAAATTCATCTTGAATAGGGGCTGGGTAAA
ATAAGGCTGAGACCTACTGAGCTGCATTCTAGGAGGTTAGGAATTCATA
GTCACAGGAGGAGATAGGAGGTGGCACAAGATACAGGTAGCGAAGACCT
CGCTGATAAAATAAGTTGCAGTAAAGAAGCCAGCCAAAACCTCACAAAGCC
AAAATGGTGATATGGTTTGGCTCTATGTCCCCACCCAAATCTCATCTCAA
ATTATAATTCCATAATCCCCACATGTTGAGGGGAGGACCTGGTTGGAGG

FIG. 3 (25 of 52)

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CGATTGGATTATGGAGGCAATTTCCCCCATGCTGTTCTGGTGATACTGAG
TGAGTTCTCATAAGATCTAATGGTTTTATAAGTGTGGAAAGTTCTCTCT
ACACACATGCTCAGACTCTCTCTGAGCTTTATGAAGAAGGTACTTGCT
TTCCTTTCTGCCATGATTGTAAGTTTCTGAGGCTTCCAGCTATGCAGA
ACTGTGAGTCAATTAACCCGTTTTCTTTATACATTACCAGTCTTGGGCA
JTTCTTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT
GTCCTCACTGCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG
ACACTCCCACCATGACCCCAACAGTCATGCCTGTGCCGGTCTCAGCACC
TGACAGTTTACAGATGGCATAGCAACGTCTAAAAGGTACCCCATATGGAC
TAACAAGGGGAGGAACCCCTCAGCTCTGGGAAGTGCTACCTCGTTCCTCAG
AAAGCTTGTGAATAATCCACTGCTTGTGTTTAAACATATAATTAAGAAATAAC
TATTAAGCATCCTTAGTTTACAGCAGCCCAAGCTGCTGTTCTGCCTATGGAG
TAGCCATTCTTTATTCGTTACTTTCTTAATAAAATTGCTTTTACTTTAC
TGTATGTAAGTCTGCTGGAATTCTTTCTGTACGAGGTCCAGAGCCCTCTC
TTGGGTCTGGATCGGGACCCCTTTCTGGTAACATTTTGACCAATTTCTCC
CTTCTGGAATGGGAATGTTTACACAATGACTGTATCACTTTTGAATCTTG
GAAGTAAATAATTTGTTTTGACTTTACAGCCTCATAGGTGGAAGGAACT
TGACTTGAATTTAGATGAGACTTTGGACTTTGGGACTTTTGGGTGGGG
CTGGAATGAGTTAAAGTTGGGGGGATTATTGGGAAGGCACGATTTTATT
TTGCAATATGAGAAGCACATGAGATTGGGGGACCAAGGTGGAATAATA
TGTTTGGATGTTTGCCCCCTCAAATCTCACATTGAAATGTAATCCCA
GTGTTGAAGTGAGGCTGCTGGAATAATGTTTGGATTACAAGGCTGTGAG
CACATTGGATAAGACGTGTAGGNCCC

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CGCAGCTCGCTGGTTAATTTCTGTGGCTCCTGTGACCACTATTATAGCACC
AGGTCTATGACCAGGAGAATTAGACTGGCATTAAATCAGAATAAGAGATT
TTGCACCTGTAATAGACCTTATGACACCTAACCAACCCCATTTATTAACA
TAAACAGGAACAGAGGGAATACTTTATCCAACCTCACACAAGCTGCTTTC
CTCCCAGATCCATGCTTTTTTTCGTTTTATTATTTTTTAGAGATGGGGGCT
TCACTATGTTGCCACACTGGACTAAACTCTGGGCCTCAAGTGATTGTC
CTGCCTCAGCCTCCTGAATAGCTGGGACTACAGGGGCATGCCATCACACC
TAGTTCAATTCCTCTATTTAAATATACATGGCTTAAACTCCAACCTGGGA
ACCCAAAACATTCAATTTGCTAAGAGTCTGGTGTCTACCACTGAACCTAG
GCTGGCCACAGGAATTATAAAAGCTGAGAAATTCTTTAATAATAGTAACC
AGGCAACACCATTGAAGGCTCATATGTAAAATCCATGCCTTCTCTTCTC
CCAATCTCCATTCCCAAACCTTAGCCACTGGCTTCTGGCTGAGGCCTTACG
CATACCTTCCGGGCTTGACACACCTTCTTCTACAGAAGACACACCTTG
GGCATATCTTACAGAAGACCAGGCTTCTCTCTGGTCTTGGTAGAGGGCT
ACTTTACTGTAACAGGGCCAGGGTGGAGAATTCTCTCTGAAGCTCCATC
CCCTCTATAGGAAATGTGTGACAATATTCAGAAGAGTAGGAGGATCAAG
ACTTCTTGTGCTCAAATACCACTGTTCTCTTCTTACCTGCCCTAACCA
AGGAGCTTGTCAACCCCAAACCTCTGAGGTGATTTATGCCTTAATCAAGCAA
ACTTCCCTCTTCAAAAAGATGGCTCATTTTCCCTCAAAAGTTGCCAGGA
GCTGCCAAGTATTCTGCCAATTCACCTGGAGCACAATCAACAAATTCAG
CCAGAACACAACCTACAGCTACTATTAGAATCTATTATTATTAATAAATTC
TCTCCAAATCTAGCCCTTGACTTCGGATTTACGATTTCTCCCTTCTC
CTAGAAACTTGATAAGTTTCCCGCGCTTCCCTTTTTCTAAGACTACATGT
TTGTCACTTTATAAAGCAAAGGGGTGAATAAATGAACCAAATCAATAACT
TCTGGAATATCTGCAACAAATAATATCAGCTATGCCATCTTTCACTA
TTTTAGCCAGTATCGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT
CTTCCCTGTAAATTTCCCGTTTTGACGACGCACTTGTAGCCACGTAGCCA
CGCCTACTTAAGACAATTACAAAAGGCGAAGACTGACTCAGGCTTAA
GCTGCCAGCCAGAGAGGGAGTCATTTCAATGGCGTTTGAATCAGCAAAGG
TATTGTCTTCACTCTCTGGCTATTAAAGTATTTCTGTTGTTGTTTTTC
TCTTTGGCTGTTTTCTCTCATATGCCCTTCTCTAAAGCTACAGCCTCTCC
TTTCTTTTCTGTTCCCTCCCTGGTTTGGTATGTGACCTAGAATTACAGTC
AGATTTCAAAAATGATTCTCTCATTTTGGCTGATAAGGACTGATTCGTTT
TACTGAGGGACGGCAGAACTAGTTTCTATGAGGGCATGGGTGAATACAA
CTGAGGCTTCTCATGGGAGGGAATCTCTACTATCCAAAATTATTAGGAGA
AAATTGAAAATTTCCAACCTCTGTCTCTCTTACCTCTGTGTAAGGCAAA

FIG. 3 (26 of 52)

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TACCTTATCTTGTGGTGTTTTGTAACTCTTCAAACCTTTCATTGATTG
AATGCCTGTTCTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA
TAAATAAAACATTCTAAAAGAAGTTTACGATCTAATAAAGGAGACAGGTA
CATAGCAAACCTAATTCAAAGGAGCTAGAAGATGGAGAAAATGCTGAATGT
GGACTAAGTCATTCAACAAAGTTTTTCAGGAAGCACAAGAGGAGGGGCTC
CCCTCACAGATATCTGGATTAGAGGCTGGCTGAGCTGATGGTGGCTGGTG
TCTCTCTTTGCAAAAGTCAAGATGGCCAAAGTTCCAGACATGTTTGAAGA
CCTGAAGAAGCTGTTACAGGTAAGGAATAAGATTATCTCTTGTGATTTAA
TGAGGGTTTTCAAGGCTCACCAAAATCCAGCTAGGCATAACAGTGGCCAGC
ATGGGGGGCAGGCCCCGAGAGGTTGTAAAGATGTGTACTAGTCTGAAAGTC
AGAGCAGGTTTCAGAGAAGACCCAGAAAACTAAGCATTTCAGCATGTTAAA
CTGAGATTACATTGGCAGGGAGACCGCCATTTAGAAAAATTATTTTTGA
GGTCTGCTGAGCCCTACATGAATATCAGCATCAACTTAGACACAGCCTCT
GTTGAGATCACATGCCCTGATATAAGAATGGGTTTTACTGGTCCATTCTC
AGGAAAACTTGATCTCATTAGGAACAGGAAATGGCTCCACAGCAAGCTG
GGCATGTGAACCTACATATGCAGGCAAATCTCACTCAGATGTFAGAAGAAA
GGTAAATGAACACAAAGATAAAATTACGGAACATATTAACTAACATGAT
GTTTCCATTATCTGTAGTAAATACTAACACAACTAGGCTGTCAAAATTT
TGCCTSGATATTTTACTAAGTATAAATTATGAAATCTGTTTTAGTGAATA
CATGAAAGTAATGTGTAAACATATAATCTATTTGGTTAAATAAAAAGGAA
GTGCTTCAAACCTTTCTTTTCTCTAAAGGAGCTTAACATTCTTCCCTGA
ACTTCAATTAAAGCTCTTCAATTTGTTAGCCAAGTCCAATTTTTACAGAT
AAAGCACAGGTAAAGCTCAAAGCCTGTCTTGATGACTACTAATTCAGAT
TAGTAAGATATGAATTACTCTACCTATGTGTATGTGTAGAAGTCCCTAAA
TTTCAAAGATGACAGTAATGGCCATGTGTATGTGTGTGACCCACAACAT
CATGGTCATTAAAGTACATTGGCCAGAGACCACACTGAAATAACAACAT
TACATTCTCATCATCTTATTTTTGACAGTGAAAAATGAAGAAGACAGTTCT
CCATTGATCATCTGTCTCTGAATCAGGTAAGCAAATGACTGTAATTCTCA
TGGGACTGCTATTCTTACACAGTGGTTTCTTCATCCAAAGAGAACAGCAA
TGACTTGAATCTTAAATACTTTTGTTTTTACCCCTACTAGAGGTCCAGAGA
CCTGTCTTTTATTATAAGTGAGACCAGCTGCCTCTCTAAACTAATAGTTG
ATGTGCAATTGGCTTCTCCAGAACAGAGCAGAAGTATCCCAAATCCCTGA
GAACTGGAGTCTCCTGGGGCAGGCTTCATCAGGATGTTAGTTATGCCATC
CTGAGAAAAGGCCCGCAGGCCGCTTCACCAGGTGTCTGTCTCCTAATGTG
ATGTGTTGTGGTTGTCTTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT
CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGAGAA
GTCTACAGCCACTCATCAATCTGTGTTATTGTGTTTGGAGACCACAAATA
CACACTATAAGTACTGCCTAGTATGTCTTCAGTACTGGCTTTAAAGCTG
TCCCCAAAGGAGTATTTCTAAATATTTTGGAGCATTGTTAAGCAGATTTT
TAACCTCTGAGAGGGAACCTAATTGGAAGCTACCACTCACTACAATCAT
TGTTAACCTATTTAGTTACAACATCTCATTTTTGGAGCATGCAATAAATG
AAAAATCTTCTTAAAAAATCATCTTTTATCCTGGAAGGAGGAAGGAAG
GTGAGACAAAAGGGAGAGAGGGGAGGGAGCCATGAAACACCAGTTACC
TAAGACCAGAATGGAGATCTTCTCACTACCTCTGTTGAATACAGCACCT
ACTGAAAGAACTTTTCAATCCCTGACCATGAACAGCCTCTCAGCTTCTGTT
TTCCTTCTCACAGAAATCCTTCTATCATGTAAGNTATGGCCCACTCCAT
GAAGGCTGCATGGATCAATCTGTGTCTCTGAGTATCTCTGAAACCTCTAA
AACATCCAAGCTTACCTTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG
GGAAGGTTCTGAAGAAGAGACGGTTGAGTTTAAAGCCAATCCATCACTGAT
GATGACCTGGAGGCCATCGCCAATGACTCAGAGGAAGGTAAGGGGTCAAG
CACAATAATATCTTTTACAGTTTAAAGCAAGTAGGGACAGTAGAAT
TTAGGGGAAAAATTAACGTTGGAGTCAGAATAACAAGAAGACAACCAAGCA
TTAGTCTGGTAACTATACAGAGGAAAAATTAATTTTATCCTTCTCCAGGA
GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTTGCTCACAGCCATTA
TTTCTTAGCCATATTGTAAAGGTCGTGTGACTTTTAGCCTTTCAGGAGAA
AGCAGTAATAAGACCCTTACGAGCTATGTTCTCTCATACTAECTATGC
CTCCTTGGTCATGTTACATAATCTTTTCTGTGATTGATTCTCTACTGT
AAAATGGAGATAATCAGAATCCCCCACTCATTGGATTGTTGTAAAGATTA
AGAGTCTCAGGCTTTACAGACTGAGCTAGCTGGGCCCTCCTGACTGTTAT
AAAGATTAAATGAGTCAACATCCCCCTAATCTCTGACTAGAATAATGTCT

FIG. 3 (27 of 52)

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GGTACAAAGTAAGCACC_AATAAATGTTAGCTATTACTATCATTATTAL
 ATTATTTTATTTTTTTTTTTGAGATGGAGTCTCACTCTGTTGCCAGGC
 TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGT
 TCACGCCATTTTCTGCCTCAGCCTCCCGAGTAGCTGGGACAACAGGCAT
 GTGCCACCATGCCAGCTAATTTTTTTGTATTTTATGATAGATGGGGTT
 TCACTGTGTAGCCAGGATGGTCTCTATTTCTGATCTCATGATCCGCCT
 GCCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGGCCCG
 GCTATTATTATTATTACTACTACTACTACTATATGAATACTACCA
 GCAATACTAATTTATTAATGACTGGATTATGTCTAAACCTCACAAGAATC
 CTACCTTCTCATTTTACATAAAAGGAACTAAGCTCATTGAGATAGGTAA
 ACTGCCCAATGGCATAACATCTGTAAGTGGGAGAGCCTCAAATCTAATTCA
 GTTCTACCTGAGTAAAAAATCATGGTTTCTCCTCCATCCCTTTACTGTA
 CAAGCCTCCACATGAACATAAAACCAATATTCTGTTTTTAAGATAATA
 CCTAAGCAATAACGCATGTTACCTAGAAGGTTTTAAATGTAACACAAT
 ATAAGAAAATAAAAACTACTCATATCGTCAGTGAGAGTTTACTACTGCCA
 GCACTATGGTATGTTTCTTAAATCTTTGCTATACACATACCTACATGT
 GAACAAATATGTCTAACATCAAGACCACACTTTTACAACCTTTATATCCA
 GCTTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC
 C

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GTATTCTATTCTCGGTTATAACACAATCACAGTGATTTGTCATATCTTTC
 CAGGATTTGTTAATTTCACTTCTTCAGCTGTTTCCCCCTTGTTGGCTGGA
 ACTGATTTTCTATCTTCTGGGAGAATCTTCAGCAAGCCAACCTCAGGATTT
 GTTGGGTGCATTTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATTT
 CCTCTAATTACCGAGCAATGTAAATGAGGAAGTCTGATTGTGTAAAGGT
 GTTAAACTTTTGTGTGACGGCAAACTTTAATACCATGAATAGAGATTCC
 AGAATTTTCCAACCTCTAACGGGATTCTTTCACTCCCTGACATTAGAAT
 GTTAGAAAATCTACCACAAAACATCTGTGAGGCTATCTTACAAGGCCCGT
 TTTTCAAAATAGGTTTTTACAAGGATTGCTATTTGGGATGATAGTTTCAG
 AAAGGCGCTATCAAAGTTAATTGATGATGTGTGCAAGCTGAAAGTTATAT
 GTTAGAACTAGCAGTGATTTCAAAAATATCCCTTTTAGGCTTTTGTCTAA
 TATATCTGCTCATTTTCAAAGTTCCCAATATTATAAACTTTTAAAGCA
 GAAAGAAGAACCCTCCATTTCTGCTGGCCCCCTTCCCTGTTCAACTAAAA
 GTATTTTCCCAGGCAATGCTATCCCAGGACTCACACTCCATCCATCCATC
 ACCTACCATAAGTTCTTTGAAGGGCTCATTCTGAGCGCTTCCCTGAGTGCC
 TGGGATCTGTTATTTCTCTCCATTTCTGCTGCTGCATGGTAGTCCAAGTC
 CTCCTCCCTTTTCCCTAGGCCATTTGAATCATCTGCTAATTGGTTTTCC
 TGATTGCCACGGAACTTCCCTCCATCCCTTCCCTCACATATCAGCCACAGA
 AGTATCTCCAAAAAGCAAATCTGGTGACATGAAGCCCTTGCCACAAAACC
 ATTCATTACTGGTTCCACACCTCCTTTGTGGATAAGTTCAAGCTCCTGAG
 TGTGGCAAGCAGGGCCACCTGGAATCCCCCTGCCCTCCTCTCCTATCCCA
 CGCATCAATCTTTCTGTCTATTTGCAAGTTCCTTGAATGTGATATTCTTT
 CTAGTCTCTGTGCTTTTGCAACCTGTTCTTCTGACTGGAACTCCTT
 CTCCTCCTTGTAGTTTGGCTAATTTCTAGTCTTTCAAGACTCAGCTCATG
 CTTACCCCCCTTATAACAAGTCCTTTCCCAAGCTGGGTGGTGGATGCTC
 CTCTGTGCTGTGTGAGTCTTGAAATCCTCAGCAAACCTCAGCTTTGTTT
 GCTTGTCTCCCTTGTCTGCAATGCACCTGATTCAGGGCTGGCATATACTG
 TTCACCTCCATGACTGGCTCATGGTGGTGCTCCGTGAATATCATCCACCC
 AAACGGATGAGAGCTACCATGCCATCACTTGTGACTTCCATCTGGAGCTA
 ACCTCCCCCGACAGGAAAGCGTTTCTTAGGAAAGAATATCTTTGGGTTA
 AATAGAAGTAGAGACTACCAGAAGCACTATGTCCAGCTCAGAATGAACT
 GCTCAGTAAGCAGCCTTGTCAATGAGGAGGCAGCAGGCCAGCCCCAGAGG
 CCTCAAAGTGGGAGAGTAGAGAAGCGCAGTTCCTGCCACAAAGGCACAGT
 GGACACCTTGCTCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT
 CCATGGGAATCTGCACCTTTAATAAAGTTTTATGGGACAGGAAGGTGAC
 TGGCATTGACATTGTAAACGAGGAATGGGTGGTGCCACCTTTGCTGTGTCT
 TACCAGAAATACCTGTGGCAGGTAAATTTCTAGAGAGACCTCCCATTTTC
 TCCCATATAGCAATTTTGAATGTTTCTGAGGGCTTTCCAAATTCATCT
 GGGAAACATAGGAGTTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA
 AGAAAGTAGCTTTTGAATGACTTACATTAGCCATTATCCATTACAGCAC

FIG. 3 (28 of 52)

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ACCAGGCATTGAGTTTGGAGGGGTGTGTGTGTGTGTGTGCGCGCGCGCGTGTG
CGTGCGATGAGTGCATGCGCGCGCGTGTACATAGGGGAAGGGAAACAAAAC
AAAAGTACACAAGACATGATAGTTGTCTCAAGGAGTTTTTGCAAATGTT
CACAATTTAAGAGAATATGCTGTGCTGTGGCTGGTGTATAAACCAACTGC
TAGGGAGAGGCCCTTCCACACACACTTGGGGCAAATGCGACCTTAGGACT
GCCAGTGGAACTCTGGGCATGCTGTTTGTGGTCGATAAACCCCTGGTCCCTT
GATCAGGGACCTATGTTTACTTTTCTCTCCCTGGAAGTCTTCATTAGTG
GGCATCCAGAAGGTCTTGACAGGGCAGAGGGAGGCACAAAGACAAGAGT
TTGAAACCAGCCTGGACAACAAAATGAGTTTCTATCTTTACAAAAAAAT
TTTTAAAAAATTAGCCAGGTAGGATTGCATGTGCCTGTAGTCCCAGCTAT
TCAGGAAGCTGAGGCAGGAGGATTCCCTGAGACCAGGAATTTTGAGGCTG
CAGTGAGCTATTAAGTTGGCGCAAAAGTAATCGTGGTTTTTATCATTAAA
AGTAATGGCAAACTTTTAATGACAAAAACCGTGATTACTTTTGCACCAA
TTTAATATGATTGCACGACTGCACTGTGCTCCAGCCTGGGCAACAGAGTG
GGACCTGTGACAAAAATAATAATAATAATAATAATGTAACATGTAAAAAA
ACCCCAAAAAACAAAAAATGGGTGTTGAGACCCCTGAATTGAGGAATAA
TAGGAAGGAGTGTGATTCTGTGTGTGCATGCATGGGTGTGCACCCTCAGT
GCCTGGGTGGCTTACCCTGGGCTAGTTCCAGGTGGCAAATGGTTTTCTCC
AGCTGGGCTACCACCATCTTCCCCCAGGGCCTGTCCATGATTTGGTGGC
AAGATACCTATGGACTAGAGTCCCTCCTCAGAGGAAAGGCTCCTCCCATT
TCTCTGGCTTTTCAAGTAGTAGTCCATGACTTCAACAGGTCCCCAGTGCAA
TGTTATGGGTAGTTTAGGTGGGGTCTCCTCTGAGAGCCTCCCATAGCCC
AAAAGGCCCTGTCTAGCTGGCACTGCATCTCCCTCTTCCCAGCTCTCAG
CCTTTCTCTTTGCTCATCCCACTCCGCACAGGCTTTCTGCCTGATCCTTG
GATGTGTCAATCTGCCCCCTAAGGGATGCAAGGCAATTTGTCTTTTATT
ATTAAGATCTCTCCTGAGGCCACGTGTGGTGGCTCACACCTGTAGTCCTA
GAACCTTTGGTAGGCCAAGGTAGGAGAATTGCTTGAGCTCAGGAGTCCAG
GCTGTAGTGAACCATGATTGCACCATGCAATCCAGCCTGTGTGACACAG
CGAGACCCTGTCTTTTTTCTTTTTTTTTTGGAGACAGGGTCTCGCTCTGT
CATCCAGGCTAGAGTGCAGCGGTGTTTTCTGTCTACTGCAGCCTCAACC
TGCAACATTTTTTGTAGAGACGGTGTCTTGCTATGTTGCCAGAGTGGCCT
CAAAGTCTGGGCTCAAGAGATCTTCCACCTCAGCCTTCCAAAGTGCTG
GGACTACAGGCGTGAGCTACCGCGCCCAACAAAGACCCTGTCTTAAAAG
AAAACAAAAATAAACAACTCCCTCAAGTCTTTTTTTTTTTTTTGGAGCGG
AGTCTCGCTCTGTGCGCCAGGCTGGAGGGCAGTGGCGCAATCTTGGCTCA
CTGCAAGCTCTGCCTCCCGGGTTCACGCCATTCTCTGCCTCAGCCTCCC
GAGTAGCTGGGACTACAGGTGCCCGCCACCACGCCTGGCTAATATTTGT
ATTTTTAGTAGAGATGGGGTTTCACTGCGTTAGCCAGGATGGTCTTGATC
TCTCAGCTTGTGATCCGCCCGCTCGGCCTCCCAAAGTGCTGGGATTAC
AGGCATGAGCCACCGCGCCAGCCAGACCTCTTGAGTCTTAAACTCCTCT
GTAGTCCAGCCACCCTTTAGCACATGACTCTGTTAATTTGTTCTCACT
GTCTGAAATCATCTCCTGTCCACTCTTGACTGACAGGTCTCTGCACTAGC
CCACTGCTTAATCAGAGTAGGTCCCTGTCAACTTATTCATATTGTGTCCC
CATCTCCTTCCAAGTCTCACTTGCTGGCTCCTGTCTTAGTTTTAGTCC
CCATTCTTCAAAGAACGTGAGCCCTGGAAAGTATTTAGTCATTTAGTTC
AGTGCCTTTGGATGGGAGGATCACATCCCTGGGTCCCGTCTCTGCAGACTG
TTTTGCTCTAGCTGACTAGGCAGGATTCCCTGCCTTCTCTCACTTCGGCA
TGGGACTTCTTCTGAAATTGCTGCTCAGTCAAGAGAATGACCTTCCCCA
ACATAATCCTACTCCACAGGGACTTAAAGGTGTGTGAGAGATCTCTTGCT
CATCTTTCTGGCCAGGTGCCAACGTCAAGTTATAGCCAAGGGACAAGACT
AGTTAGCAGATCAGGCAGGTCTTAGACCCCAAGCGTAAGTGCCAGACTCT
AGCTGCAGTTGTTCTGCCCACTGGGCGTTCAGGTGGAGAGAGGGCAT
GGCACTACACTGAGCTCTCGGCGAAACCCAGGACTCTGAAATCTCGGTGT
CAGCCACAGGCCACTCTTTTCAGCAGGACTTCAGTCAGTCTGTCACTAG
GCTGTGAGCACATGGTAGGCTTTACCCC

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AAGGAGTGTGCTTGCTGATAGCATGTGTGANGGGACGAGGAGTAAATAAT
TTCTGCCTTCAAGAAATTGCAAACTAGTAATGGAGATAAAATCAACAGAG
GAACAAATTAGAGTATAAGGTAAAATCTAAGGGCCATAAGAGAGGAGAAGA

AGTATGGGAGTTGAGAGGAGGGGGTAAATGAGGGGAGTAGGTGGGTAGA
AAAGGTTAAAAGTAAATAATGATGGGAAGGAAGACAAAAAGACGACAGGG
GTGCCAAAGGACTCTTAACCTCATCTGAACGGAGTTGCCCTGTTTTGCTC
TCTGATGCTCATGTATCTATCCTTAGAGACAGCTTGGCGGGCAATGTAGA
GCGTAGGGGCTGACATAGGGGGTGGAGTCCACCTCCGTGACTTCTAGC
AAATTAGCAAACCTTTGCTGCTGCTAAGCCTATAAGGCGGACAGAAATGCC
ATCTTTAAAGCTTGTTATGTAAAGTGCTTAGGACCTCGTAGGCATCAACA
GGAATAATGGATGAAACAAAAACAACGGTGCGTATCTTGGAGAAAGTGGCA
TCTGAGCAGGAGTATTTTGAAAGGTAGGAAAGGGCTCCAAGCACATCTAA
GAGATTAGGGAACGAGAAGCCTTAGCCCTGGGTGCAGATTTAACCAATC
AAGTTCTAACCAACCGCAGGCTGAGAGGTGTGGAGTGAGAGCCCCGCCAGA
GGCAGGAGACCCGGGCTTCGGCCAGACCCCGCCTCCTGGTACAGAGACC
ACGCCCGGCTCTGCCTGGAGCCAAATGTGGATCAAAACAGCGCGCAGCTT
CCCACTGCTGGTGAACCCGAGCAAGGGGCTCAGTTTCTTTATCCGGA
ACGTGGTGACAATGACATCTCTTTGCAAGGCTGCTGCAGGGCTTTCTGGA
AATACGCCCGTGAGGTATCTGGGCTGCGCACAGCCTCCCCCGCCAGGA
CCCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGATGGAACCGC
CCAGGGGAAACTTAGGCAGGCGAGCGGACGGGCACCTCCCGCGGACGAA
CTCACTCGGTGGCCTCCTACTTCCCGCGCGTGTCCAACGCCCTGAGAAT
AACGGGAACAGCGGTGCTACTCACCGACAGCGGCAGCAGCGGTAGGCCCG
GGCCCCACCATGACTCTTCAGTGACAGTTTTCTTCAAACGCCGCSCTG
TAGCCAGGACCGCGTGCCGCGCGTCCACGCGTCTCATTGGCTCCTGCG
GTTTTGAAACTCGCTAGTCGTGAGCAGCGGAGGGCGGGAACAACAGGCAAT
AGGCTCTTTGCGGTTGGCTCTGGCCTTGAGAACCCGACCTTGGGGCCCTT
TGATTGGAAGACGTGCAGCGCACCTCGGCATTGAGGGCGGCTTCTCGG
GGCGCGGCGCGCCCGCTCTGAGTGCGCCTGTGAGTGCGCCTCCGAGTG
GGCGTGGGACCTCCGTGGGGGCTCAGCCGGGCTGGTGGTTGGGGGCG
GTTACGCTGAATCCAGCTGGGGTTGGCGCGCGGGAGTCCCTGGGCGGAG
AGACAGGGCGGTCTCCAGGATGCTGGGGCGCTACCTGATTCTGTCTCT
TTCAAAGTCTCAGACTCAGGAGCTGTGAAAAATAATATTATAAAGAG
GACATATGGGTCTTATGCATCTAAAGGCTCTAGTTCTTAGTACTGCAGG
GTGGCTCGTTTTAATTGTGGTAAATATGCATAACATCACATATACCATT
TAACCATTTTAAAGTGTTAAATTTTCAAATGTGCAGTTTAGTGGTAT
TAAGTACCCTCACATTGTGGCACAGCCACCACTACTGTCTTTCCAGAAC
TTTTTCATCTTCCCAAATGAAACCCGTGTACCCGTCACTAACTCCGCACTC
CTCCCTCCCCCAGCCCCAGGCAATCACCATTCTAGTTTCTGTCTCTATGG
ATTTGACAACTGTAGGTGCCATATAAGTAGAATCATGCAGTATTTGTTCT
GTGACTGGCTTGTTCCTTAGCATAAAGTATTCAAGGTTTATCCATGTG
TAGCATGTCTCAGAAATTTCTTTCTTTAAGGGGAATAGCATTTCGTT
GTGTGGAGATGCCACATTTTGCTTCTTGGTCCATCCCTCTCCGACACTT
GAGTTGCTTCCACTTTTTGGCTATTGTGAATAATAATATGAACATGAATG
CACAAATAACTCTTTGAGACTCTCTTTTCACTTTTTGGGTATATACCA
CGAAGTGGTATTGTTGGATCAAACGGCAATTCTATTTTTAATTTTTTGAG
AAACTGCCCTTACTCCTCTCACGGTGATCTCTGTTCAAGGTATATTTTCG
ATTTACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAAACGC
AGGCCTAGTTTCTCCTAGTTACTAGGAGATCGCAGGCCTCGTTGTCCTGA
ATCCCTAGACACACTTCATTCCCTTGTTTTAATCCTAAATTTTTTTCT
TTTGAAGTTTGCTGTTTCTATCTATTCTCCAGTTTCTTAAAGAGGTCTG
GAAAATGCTTTGGCTCCTTGTGTATGAAGTTTCTCTCCATGGATGCT
GGAGAAGTCGTGTGTGGAGGGGAGTCATATCTGGGCACCTGTTGGCCAG
GTTGAGCTTACCAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG
CCCTTCTCTTAGCCGTAAATAGGGAGTTTGAAGAGAGCCAGGGTTTCT
GGATTTATGCATTTTGATATTTCAATAGTGTATTAAATGTTTAAATAG
GAAACTGATCATTATTTTGTAAATGACTGAGAAAGGGACTCCTTCACC
AACAGTTTCAGAAAAGTGAAGGCGTTTTGTTTTGGTCTTTGTAGAATCT
AGGTGGTTGAATGCATGTGAGTTGTAGAAGTCACCTTGCCGTGATATCCCA
CGCAGTGCTGGAGTATTCACAGACCCCATGTAGGTACTGCACCTTTGCA
GGTATACTGCTGGTGTGGTGAGCTGCCTTACCTGTCTGTTATTGGAGA
CCCTGCTTATTAGGAAACTTAAATGAACTCAAATGAGCTTCTTGCTT
ACTGGTCTAGTCCCTTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTTT

FIG. 3 (30 of 52)

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TCCATCCCTTTGGGTATTTGACGGTCTATTTTGTAGGACACAAAATGTGGG
AAAAATAGCTAGGCAGGTTTAAAAATTTCTCAACTCTACCAAGCATGGTGGC
TTATGTCTGTAAATCAATCCCAGCACTTTGTGAAGCTGAGGCAAGAGGATT
GCTTGAGCCTAGGAGTTTGAGACCAGACTGGGCAACATAGCAAGACCTCG
TTTCTTAAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA
CACACCTGTAGTCCCTTCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG
AGCCCAAAAGTTGAAGGATGCAGTGCACCTGTGGTCATGCCACCGCACTCC
AGCATGGGAGGCAGAGCAAGACCCCTGTCTCCAAATAAATAAATAAATAA
ATTCTTAACTCATTATCAAAAGTATCCACTGTAGCTTTCCATCATCTCTGG
TGT
GGCATGATCTCAGCTCACTGCAGCCCCACCTCTCTGGCTTAAGCGATCA
CCCACCTTCAGTCAACCATCTGGGTAATTTTGTATTTTGTAGAGATGG
GGTTTTGCCATGTTGCCCCAGGTTGGTCTTGAACCTCTGGCTCAAGCGAT
CCATCTGCCTCCATCTCCTAAAGTGTGGGATTACAGGTGTGAGCCACCA
CACCAGGACAATCTGGTGGCTTTTAAACGGTTTCCATTGCTCTCAGGCT
AATGACCTATAAGCCCCCTGCGGGCTTGGCCTTTTACTCCCTEAGCATTAG
CCACCTCCCTTAGCCTTAGCCCACTACTCTCCCTTGCTCAGTGTAT
CCAGACACTTTGTTTTTCTTTCCATCTCTCTGTCTGGGAATCCA
ACCTTTCTCTCATTTCTCTAGTTGATTATTATTATTTTACTCTAGCA
GCCTTATTGAGATATTTACATACCGTACGATTCTCCCACTTACAGTGTAC
AATTCAATTTTCTAATTTTCTATCACCCTTAAAGAAACCTTACTCA
TTAGCAGTCACTCCCAATTTCTCCCTCTCTCAGCCCTAGAAACCATGA
ATCTACTATCCATCTCTATAGATTTGCCTCTCTGGACATTTTATATGTATG
AAATTATGCAATTTGTGGTCTCTGATGGGCTTCTTTTGTACCAAAATAT
CATGGGTTTGTATCTAGGTCCTGCTGCTCGCTGCACAGAAAGCCAGCCACT
GAGATGACAAGTATTGCCAAGGAAGAAGGCTTTAGTCAGGTGCTGCAGCT
GAGGAGATGGGGGCTCAATCTCAAATCCATCTCGCTGACCTAAAACAGG
GGTTTGGATAGCAGGGAAGAAATGTAACAATGCGTAAGAAAACAGGAACC
AGGGAGGGGCAAGGAAGCAATCCTGATGAATGAGTGGTCCAAAGTCTCAT
TGCCTGGATGTGGTGTCTGGCGAGTTTCAGTTCTTTGATACTTTTTTTG
AGAGGCCTGAAGTCTTTTCCCAGGAAGGAACCTCAAACAAAACAAATACA
AGCTTCCAGCTTTAAGACCAGAAGCGTCAATTTCTATGTTTATCCGAAAG
AACAGTCTATGGGACTATTGGTTAAGTTTCACTTTCACTTAGTATGCTGT
TTTCAAGGTTTATCCACATAGCATGTGTGAGTACTTCACTTTTATGAC
TGGGTATTCTATTGTGCGGATATACAATATTTTATTTGCCATTATCAGT
TGATGGACATCTAGGTTCTTTCCACTTTTGGCTATTATGAATAATGCTG
TTATGAACCTTTATGTATAAGTTTGTGTAGACATATGTTTTCAACACT
CATGGGTATATACCTAATGAGAGGAATTACTGTGTACATACGATAATTCTA
TCTTTAACCATTGAGGAACTGCCAGACTGTTTTCCAAAGCAGCTGCAGC
ATTTTACATTTCTACCAGCAGTGTATGAAAGTTCCAGTTCTTTACATCC
TCAACAACACTTGTATTGTTCATCTTTTAAATTACAACCATCCTAGTGG
TTGTGAAATGGTATCATTGTGGTTTTTATTTGTATTTCTTGATGACT
AATGATGTTAAGCATCTTTTATGTGTTTACTGGCCATTTGTATATCTCT
ATTGAGAGTCTTTGCCAATTTTAAATTGGGTCAGTTGTCTTCTTCCCTT
TTTTTTGAGATGGAGCCTCACTCTGTTTCCCAGCTGGAATACAGTGGTGT
GATCTCAGCTCACTGCAACTTCCACCTCCTGTGTTCAAGTGATTCTGGTG
CCTCAGCCTCCCAAGTAGCTGGGATTACACGCACCTGCCACCATTTCCAG
CTAATTTTTTTCTTTGTATTTTGTAGTAGAGACGGGGTTTACCATGTTGG
CCAGGCTAGTCTCTTTGTGACTCTTAACCATCCTTCACTCTCAGACAAA
ACATCCCTTTCTCAAGGATTGTGATTAGCTTGATTATTTGCTTATCTTTC
TCCCTGCTAGTCTGTAACTGAGGGTAGGCCACTATATTATTGTTCTTG
GCACCAATAGAACTAAATTAATGTCTTTTGAATGAATAGGGCTTTCTC
CTTTTAAAGATCCCTTCAATACAGTAACCACTATATATAAGTAGCCAC
AAGCCCATTTCAATAATACTACTAGTNTTGGCCAAACC
>Contig36
GGCTCAGCGTTACTATACTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGC
CCCCCTCGGCTTCCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCC
TGGCCTCAAATAACTATTTAAGTGAAACAAAACCTAGTATGGCACTAATGA
AAAATGTATAAATCCATAAATCGCAGAGGGATTTCAACTTACTTCTTTTGA
TTATGTAAAGGTCAAACAGACAAAAGACAATGACAAAACCTAATGCAATG

FIG. 3 (31 of 52)

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AACACTTTTGATTTAATGAACATATATTGGATATGTACCCAAGAATTAGA
GAATACATACTAGTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTG
GAAGCCTAAATTATAAAAAGTTGCTGTACGTTAGAAATAACACACAAACCC
TTGAGTCCGGAATTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTT
TATCCTCCACCACACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCT
TGATTCAAATTCATGTTCTGTGAGCTCAAATCATTCTCTCTGCTGGAA
TAAGTACTTTCATACATATTCTGCTATTGAATTCTTGTCTTAGCACCCCAT
CTACTCCAAGACGATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTT
GATTACACTTTTTTTTCTACTTCCATTATATTATTGATCACATCTGTGC
CACAGTTTTTGACTTTGTGTCTGCTTTTACTCTTTTCTAGACCCCTGATAG
CTCCTGAAGGGTTGGGTCAATTTCTTTTATTGCTCATTCTCATGGCA
CAGTGAGTGCTTAATAAATGGCTATTGACTGAAATTAAGCTGATCTAAA
TGGACATATTCACCTTCTGGGCCATTCAATCTTTCTTTCTATTGGAACCA
GGAGATGGGGAACCATAAACAAAGGTAAGGTTGTGCCATGTGAAAGAAT
GGAACCTTCCCTGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAA
AATCTTCCATTTTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG
TGGGACTTTATCATGACGTTATTTTGGGGACTTATAGCTGCATCATTTA
CCCCATATACATTTTACCTTTAGTGTAGGGAAGTGAAGACAGGAATTTGT
TGATGCAGACTCTTGCTAATGAGGCTAACACTTGGAGAATTTTATCATG
CATTCAAGAAGCTTGTTTTACATTTCTTCATTAATACTTTAGTTGGTGGT
TTAGCTTTAGTTGTAGGCTTATCAGATATTTGGAGATATCTTCATRAACG
ATGGCTTTGGTTTTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATA
ATCAAACAGCATGGCCATTTGTTTTGTAAGGCCTTCTCTAGAATATGACG
GTAAATCTACGTGTGGAAAAATGCTTATTCTCTGTCTCTATAAATGT
GAATCTAGTTTGTCTTCAAAATGAAATCAAGTGATTAAATGTAGTTTTC
TAAGAAGATAAATGGAGCAAAGCACTCTGTGTTTTACAGTGTTGGAAATC
ACTCATCCCTCATAAAAGTGTCCCACTGATCCTGACTCATGAATGAA
TTAAATAAAGAGTTAATAACATCAATTTACATTTTAAAGACACTTTCCC
ATGTTTTAGACTATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAG
AGTTGGCTGTTTTTGTCTGTCTGTTGTTGACGTATTTCAAAGCCATATCT
AATTTTGTGTGCAAAATGCTGAATTTACAAAAATGTTGAGTTGTGTAG
TGTGGAGAAGTACGGAGCCATTTACTGAAAGGCTGGGGGAAATGACGAG
ACCCTGAGATAAGGCAGTAGTGGTGCGAACAGAGTGGAAGGGAGGTAGTT
GAGATATGTTGAGAGTAGAATCAGAATGGACATAGTGAACAAGTGGATGC
AGGTGGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT
TGATCCACTGAAGTTACATTATTCAACACCACAAGGAACTAGGGGAATG
AGAAGGCATCTGTTTGGTTTGGAGTGGAAAGGCAGTGATGTAAGAGGA
CTTAATGAGTTAAAGTTTGGATATGCCTGAACCTCAATTTGATATGTGCA
TCTGATATACCTTGGGGTGACCTCCAGGCAATGGTTGAACATGTGTAT
TTCTTAGTAAGTATAGGCATCACAGACTCACATCAGTAAGGAAGCAACA
GCAAACTTGATTGGACGATATACCTGGAAGTCACTACCCTATGACTGGAG
CAAGTCTCTGTGAGTGAATGAGGATAAGAAGAATCTTGACCTTGTGGAA
TATGTTGTTAGGAATATATGTGATGAACAACATAGGATACTTCTACAGG
GCTCCACATGTAGTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTG
TAATTTATTTCCAAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAA
TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCA
CTTTGGAAGGCCAAGGCAGGAGGATCTCTTGAGCCCAGAAATCAAGACC
AGCCTGGGTGACACAGGGAGACCTTGTATCTATGAAGAATTAATAAAT
TAACCAGATGTGGTGGTGACGCCCTATAGTCCCTGCTGCTTGAGAGGCTG
AGGTGGGAGGATGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATA
ATTGTGCCACCACACTCCAGACTGGGTGACAGAGTGAGACCTTATCTCAA
ATAAATAAATAAATAAATAAATAAATAAGTACAAACCAGCAACACTAAT
CCTTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGC
AGAGGGACCTATGAGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGG
GTTGCTAGAGAGGTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCA
AGAATCCGTGAAGACTCAGACTAATTTTTTTTTTTTGCATGAGGATTAG
GTGTTCTAGGAATTTCAATGAGAGCAGGTTAATGAAGGAATGCAGGGT
AGGAGAGCTGAGGGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC
CTCAGTATGGCTCACCTGCTTCTCTGTATCTACTTAGCAGATGATCCCA
CCCCAGGCCTCCAGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGA

FIG. 3 (32 of 52)

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GGGCCCTGGAGCAGTGTAAAGGAAGACAGAGTCTTAAGAAATTGCATTAAAC.
 BTTCATGGTGCTTGGCAAGTGTCTGTCATCCTATGCCAAGCCTGATCTGAAG
 GGGTGCATGCTCATAGGTAGCTGCTGCCCAAGATTACAGCAGCTTCTTCA
 ATCCCAGATCCATGCTCTCCTATATTCAATTTTCCAGGGGTTCCTGTCTCT
 TCGACAGTGATGAGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGT
 TGCCCACTTTTCCAAATGACAATGGGGCATGGAGCTTGAGAGTGGAATG
 AGGCCCTAGGGATAGCGTGCTTAGGAAAACACTCCCAGCCTGATGTAATT
 CTGGGGGTACAATGGCATTTTCATCATCAAGACTGATGTAAAGGGTGACT
 AGCAGTGAGTTGGGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCC
 TAATCCAGACAGAGCAGAAGCACTAGTGGGCTGGTAGAGGGCTCCAGGG
 CCTCACTTAATGTCTTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCT
 GAGGACAAGCTTGGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGT
 GGCCTGCCCTGTGATGCCCTGCCCTGCCATTCTGCGTGTGATGTCTCTG
 GGGCATCTTGCCTTCCCTGCCAGACCTGTAGTTCAGCTGAGGGCATGTG
 GAGGCCAAATGGCTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGG
 GAGAACTGGAGGAGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATC
 GTCCCGGTGGAGGTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTT
 TTCCTTGGAGATGTGTGGGCATGTCTAGAGGAAATACCCAATTCCTGAG
 CCTTGAGCCCTCCAGGAAACCTTGGAAATATTAGGTTAGTCATCCCCAAGG
 AAGTCTAAGAATTCTGGTCTCACCCTCTCCTTTAATTCCCAATGATC
 CTACATGATATTAAAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGT
 GGTGGTGAAGTTTGACCTCATGATGGAGCGGAGGTTGGTTTGAACCTAA
 EAATTTAATTTATTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCA
 TACATAATTGACACATAAAAAATTGTATATGTCTACGGTGTACAATGTGAT
 GTTTGGATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA
 TACCCATTCTATCGTGTTCAAAGGAATTAAGCTCAAGCACAAAAGAGAGG
 TGCTGTTGAAGGTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGT
 CCTGGATCAGGGTCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCT
 GCTCCACTTTCCCCACATTTTCTTCTGGAGCCTCCCTAAGAAATTAGGACA
 TGGCCACTTTCTCTGCATAGGCTTCTACTTCAACAAGGACAGGGCTTGT
 GCTGCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACAC
 TGGCTGAGTGAGGAAATCCCCAGATTAACTCTTGGTTCTAAGCATCATGG
 CTGTATTTTACACGTATATGAATTACAAATTACAGCATAGTCAATAAGG
 ATTTTTGTGCTACAACCTGGAATCCCAGATTATGCAAATTGGATAGTATAA
 TATTGAAATTCCTAGGACTTTTTATTAGTTTTAAAAAATTATACAAGCTT
 AGAGTAAGAAATTAACAGTGCAAAAGAAATCACTGTGAAAAGTAAATG
 CTCTGTCTCTGCTGAGAGACAGATATTGCAGCCCAGATACTACTGGGGTC
 AATAGTTTTCTTTAAGCATGCCATTTTGATGGTTTATGGGACTTACAGCT
 CAAGAAGCTTGACACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTAT
 TAGATATGACCGTCTCATAAAGATACACACACAGACACAGCGATTGGAGA
 TATTCACTGGGGCTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGT
 TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGG
 TTAGCAGGAGCCCACTTAACATGTCTTAAGCCACCTGGAAGAGTCTTTCA
 AGGAGACCAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTTGGCCGTTT
 TTAGGTATTCTAGTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTCT
 GTGTGCCCTTTTACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCT
 GGCTCTTGAGAGAAGACAGCAAAAGCGGAATAAGAGGTCAAGGAAGCTGTG
 TGGTTGTAGGAAATCCCAGCAGAGGGCTGGGGGTCAAAGTGGTTCATGG
 TAGTGACGGTGGAGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCATG
 GGCTGCTGGTGTCTGACCGAGCTCCTATGCTCTCCTGGTTCATTTTAGG
 CTCTGTAGCAGCAGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATA
 TCAGGCAATCCAAGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGC
 AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCA
 GATTTGTGTTTTTAAGGACTTTTAACTGGGGAGCCCTCCGGGACAGATCA
 GATGAGAGTGAAATGTGCTCCGCCTTAGCC

>Cont: 337

GGGCGTTCCGAATTCCTGTAAAGGGAGAGTGGTTTTATTATTTTAAAC
 ATAGTCAAGCTGCTAAAGTATATGATATGTATAGATAGAGTATAATTAAA
 TACTTTCAACTACAGACAAAATCAGGAGAATGGAATTAACAAATTTA
 CAAATGGGTAAATGGCAGCATTTGGTTGCGCCCAACCCAGAGAAGGCAGAC

FIG. 3 (33 of 52)

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ACCAAGATTCTAAGATCAACGTTGGCCAGCAGCTTCAGACTTCAAATAGAA
TTCGTGATTATGCAATTATTTTTCTCGGAAAGTTTTCACTTCACTATATGC
TACTTGACACTTGCTTTCTTAAGACATCCCTCTATTTTTGAGATGACTAA
TTCAGCAATTCAATTTCTCTCACGCATAAGCTGTCACTCAACCCAAACCCA
CCAAGCCTGCAATCTACCTCAATAAGGTCTTGGTGTGTAAACTGACCCA
CTTCACCTAGTTCTCTAGCCCTCTCTTGACCAGACATGACTCTTTCATAA
CTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTCTGATAGTGCC
AAGTGTCCCCCACTGTTCAATTTTCCACTCCAGCTTCTAACAGGTGATA
GACTGCTTTTTGGGGGTAGGGGCACCAAAACATATAGACCTCATGTTTGG
ATGTAGACACTCCAGTTTCTTTAAATTACAACTACATATTAATAAGTACT
TCCAAGTGATATTCAGTCCAGATCTCTCCCTGGATCCCCAAACTTTGT
AAAACCCACCGCCTAGTTGATATCTTTGATGCTGACAGGCATTTCAA
TTTAATACTGTCAAAACAAAGTTATTGATTTTCATCTCTGCATCTGTGA
CAAATTTTTCTTACTTTGGTAAATAGCACCCAGGCTGTGTCACTGCCAA
GAACTTTCCACAGCTCTTGGAAATAAAATTCAAAATATTTTCCAAGGCAGA
AAGGCACAGTGTAATCTGGCTCTGCTACCTCTCCAACCTCGTATCACA
CTAGTCTCCCTGTCACTCACCCCTCCAGGAGCTCAGGTATCTTAAAGT
TTCTTTTCTTTTTTTTTTTTTTTTTTTTTTGAACAGTTTTGCTCTGTT
GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCACTGCAACCTCCGCC
TCTTGGTTCAAGTGATCTTGTGCTCAGCTCCCAAGTAGCTGCAATT
ACAGGCGCGTGCCACCACCCGGCTAATTTTTGTATTTTTAGTAGAGAT
GGGGTTTCACAATGTTGGCTAAACCGGTCTCAAACCTCTGACCTCAAGTG
ATCTGACCACTTCAGCCTCCCAAGGTGCTGGGATTACAGGCGTGAACCAT
TGTACCTCTCCTCTTGAAGTTTCTTGATCCAGACTCATTCTGCTTAA
GGTCTTGCATCTTCAGTCTCTCCCTCAAATGACACCTCCATGAAGACGCA
ATTACCTGTAATTACCGTGTCTTATTAGTCAATGTGTTGGTTTTCTGTC
TCTCCACTACAGTGTAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG
TTCCAGCACAGTGCTTAGCACACATAGGTATTTAATAACACACAGTAAA
ATTACCTTTTAGTGTGCAATTCTGAGTTTGAACAATGCATCAAGTCAT
TTAAGTCTGACTATTATCAAGCTATAAGATGGTTGCAACACTATCACTAA
TTCCCTCATGCTCTTGGTAGTCAGTCTCACCCCTAACGCCCCCTCTG
GCAATCACTGATCCGTTTTTTGTCTTTATAGTTTTGGTTTTTCCAGAATG
CCAATAACTAAGTTTTGAATGAATGAATGCTATTAACCTCTCATTTCTGAC
TCCAGAGCAACATCCATGCAATATTTATTATTTAGCCCCAAATACTGCC
CCCTCACCTTCACCTCAACCACCTACTTGATGATACAAGGTGAGACATTT
GGCATGTGCTTCTCATGTTCTTAGCATTTTCCCTATCTCCTTAGCCTT
CCTTCTAATCATAAACGAAGAGTGAACCTTCCCTTTCTAAAGGCAACTTA
CTCCTAGGACCTCGATGCCATAATTTGTTTCTCTAGTACTTTCTATATA
TACACCAACAATTAGCTCCAGAAAGGTAAAGACTCACTGTGTGCTCATC
ACTGTGTCTCTAGCGCTGGCACACTGCAGGTGCTGAAGAAACACCTAC
AGAATGAGTGAATGAATCTCTCCCTCTCTAGACTCCTTCTCTTTGTAAAT
CAAACATGTTCAACCTGCAACACAGTCTTATGACCAATCCTCTGTTGTCT
GACCTAGGCTGAGCTCCAGGGCTGGGACCCTGACTTCTTATTACCACC
TCAAGGTCTCTGCACTCACTTCTCTTTCTGCTCAGGATTGTTTTCTTCT
TGTCAACAGTCTTTTCTCAGACTTAGGTCTCAGCTCAGACATTGCTGTTG
AAAGTACTTCTACTGATCCTTTTATCTAAAGCAGCCATTCCAGCCCTACT
CTCTTGATCATAGCACCTGAATTAAGTTGTTTACTTACTGTCTCTTTCAG
GAGGGCAAGGAGCTTGGTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT
TGCTTCAACCTGCTACACTTTTTAGCAACCATCTAATTTTACATGCTCCC
TTCACTCGTCAGAAATTTCTTATTTTCTACTTCAAGCAGGTATACATAT
GTGCTTCTCCTGGGAGGCTCACCACTTCATGAGACTACATTTGGTCTCTG
GGTAGAAAGTGTACAAAATCCACTGGCTCAGTTTTAATCAATGTATGTTA
ATATTAACCAACCTGAGATCTTGATTTCCACGCCTGGCTAATTTTGTATT
TTTAGTAAAAACAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTCC
CGACCTCAGGTGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGACTACA
GGCATGAGCCAGCGTGCCCGGCTAAGATCTTGATTTCTACCATCTGAAC
TCTGTATTTGAACGACTGCTCTGCTTGAGCTTACTGGCCAAAACCTTGG
CCCACCTCAGACTCAGGGAAGTTTCTGGTTCTTCCCTGGTAACTTTTCTGA
ACTTAACCACTGGTTTTGCTTGACAAGAGATTACCATCTTCTCACTTCCTA
GCTATGTGAACCTCACTTATCTGCTCTATTGCTGTTCACTCTAGCACGGCA

FIG. 3 (34 of 52)

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CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT
TCTGTTTCAATTTCTTAAAGAAAAAAGCTATTGTAAACATACG
ATTACAGAAAATGATTTATAACATGTGTATGTACCACCTAGCCCTGTCAA
GTCTTAATATTTGTTATATTTGCTTCAAATCTTTTTTTCAGACTGTAGTTA
AAAATTACTTAGGAGCCATTATTTATGGCCTATTTCTGACCTAGTCTTC
TTGATGGTCAATTTGCCTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA
AGCAAAGTACCTTCGATCCTCTGCTGTTGCCCTCTTTTTTAATATTTGGGT
TTGTTTGGGTCCCATTTACGGTTGTGACATCAGCTTGAGTTTGGGAGCT
GTCTTTGTTTCAGAAAATGTTTCTGGGGAACAGCCTTTTTCAACTTGGAGTC
CAAAGTCTGTGCTTTTTGCTGAAAGCCATTATTGTTATGTTTATTACCAC
TGGTTCCTATTTGGTCTTATGCTAGGGGTGCTTGAATGGCTGAATTAAAT
CTGCCAACTGTCAAATTAGGCCTCTGGCTTACGGCTTTTGACTTTTGCAG
TACACATGATGTCTGAGGTATACAACTTGGCTGGACTTCTGATCTTGCT
TGATGTTTGGATGTCTGTTGTTATATTACCCTGAAGCAAACTGGGGTAT
GTTCTGGGTTTGGTGTGCTTCACTCTCTGTTTCACTAACAGGGTATGACCG
TATCTTAGTTTTCATTTGGTCTTTTCAATTGACTCTTATTAACCTTTATAT
CTTTGATGTTCTTGACTACTGGTTTCTTTGATGACTGAACCTTTACTAAGG
GTCCGAATAAAGTGAGAGGGAACCGTCTTTGAGGGTTTTACTCCTGGTCT
TGCAAGATCTGCTCCTCTAGAGAGTTGCTGTGATTTTACTGGGAAAGTCC
TGCTTTGTGTTTCTCCAACAAATGTTTATTAACCTATCTTTCAGAACA
GCACTATTAAGTGAACCTTTGCCAAGGCTTGTGTTAGGAACTAACTGTT
CTTGGTTTGAATTAAAGAGTCAGTCTTTGGCTTACTTCTGGTATATAATT
TAGGATCTGGCTTCTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCTCT
TTGTTTGTGTTTCTTTAGAAAGTTATCCAAAGATCTGTTTCAACATGGAT
ATTATTCTATAAAGTCTATACATTTACCATTTCTTGATCTGTTAACTGCT
GCTTTGTAGTTTCAATTGCTCTATATTAAGTGACCCACAGGTTTCTT
GACAGTCTCTCTGTGGTGGACTATCTAGCTTCACTGTTGAAAACCTCT
GCTGAAAAGCTTTAGACTATGGGTTAGAAGAAACACATTTTGAAGTCCGCC
TTTTGCCCAGAAGTTTTGGTGGCTCTAACTTCACTTCTGGGACCCTGCA
GTATTAGGTGGTCTGGGCTGGAGTTTAAATGCTGATGGACCTTTTAGGTTT
GACAGGCAAAACAACATGGTTGGTAACATCATTTTTGGGTCTAATAGTCT
GAAAAACAAGAAAAATACATATTAAAAAATCCTTAACATATCTTATTGT
TTTTAAATAAATACTGTGTTTAAACATGCTAAAAAAAATCATTTTT
AGAATTTCTCTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC
TAATAGGTAGTTTTTGTGTTTTTTTTTTTTTTTTTTTTTGTGACAGGATC
TTGCTCTGTCACCCAGTCTGGTGTGCACTGATGCAATCTTGGCTCATTC
AACCTCTGCTCTGGGTTGAAGCAATCTCCACCCCAACCTCGCAAGT
GGCTGGACTACAGGCGCATGTCACTACACCTGGCTACTTTTTGTATTTT
TAGTAAAGTTGGGGTTTACCATATTGGCCAGGTTGGTCTTGAATCTG
ACCTCCAGTGTATCCAGCACCTTGGCTTCCCAAGTGTGGGATAACAGG
TATGAGCCACCACACCTGTCTAACAGGTAGTTTTTACAACCTGAGTTC
TATCAGAAGTATATTAGAATCTTTTAGCTTGACAGAATTAAGCAGAGATG
CAGTGAATATACAAAACCTTGCTCTTTCAAAAATGAATTTGCCCTCAAACAG
TAGTTGTTGAATGCCTATTATATCTTAAGTGCCCTCCAAAGAACCCTGAA
AAAATACATACATAATGAACCTTATGTTAGGGTACCTCCCAACAAATCTCT
CCTAGTACTTTGTATAGCCACACTATATGTTTTTTTAAACCACTGCCTTTG
TAAACATCACAGTATCACTCAAGAACCTCTGTCTCATCCCTGGAGATCAG
TGACAAGGAGATAGGTGGCAGATGATGTGAGGCCTGAGATATGCTGCCAC
AGCTCTCAATAAACATGTAACATCTTAATAGTCATATTTGTAATAATCAGC
CAGGACAGGGTTTTAAGTTTAGAGTCTATGTTAATAATAACAAATGTTT
AGTCATGTGATTTAAGTTTGGATAAGAAAGGTAGGACTCGATTACAGAGA
ATTTTGAAACTAGGGAAGGGAGTTTAGAATTCATATGGTAAGTAATTGG
GCAAGCCACTATGAATTCCTGAGCATCTCTCATGAAAGCAATTACTCAGA
AAGGAGAATTTACAGAGATTTATGGAATATGTTTCCAGGGTAAGATATG
GGAATGCTAGAGTTACCACTCTATTTTTGATTTGACAAATATTGTGAAGA
ATCACTACATAAACTTGGCGAGTATGTAAAGGATTTCTAACCAGAACCAT
TTGGCATTGAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGTGT
GGTGTACTAGGAGTGAAACAGCGGAGTTGGAGTGGGAGGCAGAGAGAT
GGATGGTATACCCACAATGGCTATATCTGGATTAATCTTTGAGCACCAC
ATTTATATACACCTCGGATCTCTCCATCATTGCTTACTGAAGAGGTGGAG

FIG. 3 (35 of 52)

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GGACGTTGGCATGAAAGCTCCAAATGTGTTTTTTAGTTGCTTTCTTA
ATATTAAAAACGAATTGATATAATCCACAAACCATAAAAATTCACCATTTT
AGTAAGTGCACACTTCTGTGGATTTTAGTATAGCCACACTATTATACAGC
AATCACCACTGTCTAATCCAGAACATATTCATCACCCCTAGAAAGAGAC
TTGGGTTTACTTGTGGCAGTCCCTCCCCA

>Contig38

GGTCTACATGTGCTCGCAAGATTGGATATTGAAATATCAGCAAGAAATTA
AATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTTTATTGATTGAAA
AAAGTTGAATATTTCAAATATCAAGGTAGTAGTGAGATATAATAAAGAGA
GAGTCAGTTCTAAGTATAGAATTGCTGATTGAGTTAAGCTCTGTTCTCCA
ACATTTGGGCCACATTGAAGAGACCATGTAGCTGCTTTCAGCCTCGGTTT
CCTCCTTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAAC
TTATGACATGTTATCATGATTGCCAGGGCCACCTGTTTTCTTTTAAACA
TTGAAATCACTGTGCCTGAAACAGGGATTTCCCTGCCCTTTGTGCAAGCT
CCAGAAACAGGAGTCAGCCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG
TCATTTTCTCATAGCGAACACACTTCACAGGTCTTCAAGGGAGTACATT
TTCCTATAACTCACCTTAATCTCAGTTGAAGCCTCGTTTCTTATTTTGCA
CTGTGGCCAAAACTAAATCTCATTTCTTTCACGTAAACTTCAGCAATTC
AATAATAGTACAGTCATTTTATGTTTCAACTGAACCAAGTCAGGGTTCCA
CTCCTGCCTCCCTTCTGCTCTGAGGACATCCATGAAGTGGAGGGGGTC
TATGTAGCCTGGAGCTATTGGTGAGGGGCGATGGGTCCGTGGTGGTCTTG
GGGAAC TGCGGGCTGTGTCTGGCTGGTCTGGTGTCTGGTGATTGGCCTT
GTTCCACGCGGTTACGCTGCAGGACAGTTCGTGTCTTCTTGTCTTAAT
GATCAGCTTTTAGGCTCACGGGCTGTCTCTGCTGAGATATGGAATAGGA
CAGCCTCTGGATCTTCTTTAAACTCTCCTGGGGCCACAGGGGACTCTGTT
TGTGTCTGTGCCCATAGGATGATTCTGCCCAGACCTTTGCTGCCATTT
CTTGCTGTTCTGCTGTTTTTAGTCTCTGGAGGGCTTGCACTTTCTTTGGG
GTCCCTGTGGAAGCAAAGCAAAGTCTCTCCACGCTCAGATGTCTAAACG
TATCTGGGTTTTATCGTCCACCCATCCCAGAGCTCAGTCTAGAGGAGGGG
GCAGCCTTCGGGTTCTCTCCTTCTCCAGAGCCTCTTCTTTGCACCAG
GGCAGCCTCTTCTATCTGTTGGAAAGGGCTGTCTGGTTCTTGAATATAG
AGTTGCAGGTTTGGAGGGTGTAGGCTGAGGTAAGGCAAATATCACATGG
AATAAAAATTACCTGTGTCAAGGAACAACCAGAGCTGGACAGTTTTTAA
ATGTGAAAACCAATTTTATTTCAGGACTATGGCGAGAGGTGAAGTAAGACC
TCAGTATAGAAGTGGGCTCAATTCCGAATGCAGCATGGGCAAATGGGAAT
GTATAGCCTAGGAGCAGGGTGGGAACCTGTGGATGAAGAATTACTAAAAG
GGCATATCAGGGGTGAGGGGGCGTCTGGCTACACCCACTAATACTGTT
GCTGAAGAAAGCCTGGTGACATCACTGGGGAATGGTGGGGGATGAAGAA
TCCAATCAGATGGATATTGAGGATAAGGGGATCTTGATAAACTGGCTTAG
GAGGGTTTTTGCTAAAACCTGGTTTTTCATAGGTAAAGTCCACAGACAGTCT
TGGAGAAAGTTTCAGGGACCTACGGTTTGTTCGGGCAGATGCTTTGTCTC
TGTCACTGGCACTGTCACTGGCTTTCTTTAGTCCCTCCCCCTTTT
TTTTTTTCTGGAGTAGTTTTGGGAGACCAGAGGAGCAGGGAGTTAGGGAG
AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGTCTGTAGGGAAAATC
CTTAAATCCTCTAATTAAATTAATTTAATTTATTTATCTGGGACAAGGTC
TCACTCTGTTGCCAGGCTGAAGTGCAGTGGTGTGATCTCGGCTCACTGC
AGCCTCGACCTCAGGGCTCAAGCAGTTTTGCCACCTCAGCCTCCTGAGTA
GCTGGGGCTCACAGGTGTGCACTACCATGCCCGGTAATTTTTGGGTTTT
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTCGCCATG
TTGCCCAGGCTTGGTCTCGAACTCCTAAGTGATCCATCCACGTCGACCTC
CCAAAGTGCTGAGATTACAGGCATGAGCCACTGTGCCCGGCCTAAATTCT
CCAATTTTTTAAATGCTTCCCTGTTCCCTGTTCCAGATTTGGGATATTGAC
TGCTGTTAAATCAGCGATTTCTCCCTGTGGAGAGGTAGCCAATAGGAAGC
AACAAGAGTGAGGAGTCCTTATATCGAAATAGAGGGTAAGAGAAGAGACA
GATGTTATCTTGGCAGTGATTAAAGAACAGCGAGTCTGTAAGCAAAGCAA
AGCAAGGCTCCAGGTGCTGAGAAACAATGGCTTTCTGGGGAAGCGTCTG
TGTTCAAGACCTTAAGTTGGAACATCTCTGAAGATGTTTGCCATGAAGG
TTTTCTTGAAGTTGAGTCTTTTCACTAGGTAGGCGTGTGTTGGAGT
CTCTATCAAACAGATCCTGTGTTTATTAGGAAGCTGTGGTTCATAAAGCC
CCATGCTAATTTTGCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGGACA

FIG. 3 (36 of 52)

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TTCTTGTTCGGGTCA...AAGCCGTTTGCTTCTTCTGCCTTTTATAAA...
 AGCAGAGTTCGAGCTACACAGGCTGTCTGTGTGGCTGCTATTAGTTAATC
 AGAGAGTTTTTTTTTTCTTGCCTTGTCTTCTAATTTGTGACACATAATT
 AGCCACAATATGTGTTTTTCAGTTGTGACACTGGCCTGGGAAACCAAGGGA
 TGTGTAGAGTGGATTTCCTTGATTTTGCAATAATTGTGTGTTTTTCTGCA
 TCTTCTTTAAACACAAATTCATGGAAGCAAAACATGGAAGCAAAGTACC
 CTGGACATCCCCCTTCTTTATGAAATTGATTTCTCTTAAATGTAATGTT
 TGCTTGTTCCTTACTTTAAAAGCAATTTAAGAGTTTATTGAGAAAGTGA
 GCGCTGGAAACATAGATGCATAGAGAGAAAAATCTACCACCCTCAGGTCC
 CTATTGTCTTCTCTCATAAAGTGTAGTTTCAGGGCCTTTTAGAAGTTTCT
 TTTCTGCTCTGATTTGCATGTTTGTGAGTGTGCTATTTTAAGTATTG
 ATTTGGTCTGCAAATCCTATGAGAGATGGCAACAGAGTAGGGATCTCAA
 GCCTGCAGGTTGTATTAAGTCCAGCAGGGCCTTGATTTACAACAGAGGG
 TCCTTGAAGACATTCCATATATTATGCTAGGGGAGTGGCCAAGCAAACCT
 TAATGTGTCCCTATGGTGGGATATTTGGGGTTAATACCTGCCCTTCTCTT
 AATTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTGAAA
 TGTAGTCTTGCTTTGTGACCCANGCTGGATTGGAGTGCAGTGGTATGATC
 TCAGCTCACTGCAACCTCCACCTCCTGGGTCAAGCAATTCTCCTGCCTC
 AGCCTCCCAAGTAGCTGGGACTATAGGCACACACCACCATGCTGGCTAG
 TTTTTTTTTTTTTTTTGAACNGAATCTGCTCTGTGCGCCAGGCGGA
 CTGCGGACTGCAGTGGCGCAATCTCGG

>Cont:139

CGCTGSCATCCCTCATATCCATGAGTGTCTGTGGGCGCTGCCTCTGAAA
 TAAATCCTGCCTTTGTCTCCAGTTCACCTCCAGCCACCCATCCTGGGGCT
 GCACCCCTCCTCCTTCCAAGCCCTCTCCCTTCTCCTTCTGCTGCTGCTGT
 CATGTCAAGCATATGCATCAGTGGCACCAGGACATTTGAAATGCAACCAG
 TACAATTGGGCGCGGTTATGCCTACCAGTTTTCTTCTTAAACATTTTA
 TATTTATGTTTGAAAGCATGCCACCTTTCTTCACTTGCCAACTTGACAGA
 TTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT
 TTTGCACATGTAGCTTTAATTATTCTCATTATCATTATAGGAGTTATTC
 TTTGTAAAGGGTAAGTGAATTTTCCAAAACAAACAGAAATTTGGGGTGGG
 CCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACCTCGGCAAG
 TCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGTGTGTCTGC
 CCTTTATGAGGCCACCACTGTTCAAATGCTTGCCTGCAGCATTACTTGCC
 TAGGTAGTGTCTGTTTCTACTGAACTGTGAGGATCCAATTCTTTGTGGT
 CTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAGCCAGAATG
 CCAATGTATTACATTTTGTGATGAAGACCATAATTACAGTGATTGTATCTG
 CTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT
 ATGAGGTTAAATACTTGAAATTTGGACTTTCTAGAAAATCTGAATGTGA
 TTGCCATTACATACCTTTCTGGGGATGATGATTCTGTACTTTTATTTT
 AAAAGACATAGAAAATAAATAAGAAATCAGATTGCTTGGCTGGGCACAG
 TGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTGAGTGGATT
 GCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTGAAATCCCA
 TCTCTACCAAAAATACAAAAAAAAAAAAAAAAAAACAACCAAAAAGATAAA
 TTAGCTAGGTGTGATGGTGCCTGCTGTAGTTCCAGCTACTTGGGAGGAT
 GAGGTGGAAGAATTGCTTGAGCCAGGAGGTGGAGGTTTCAGTGAGCTGG
 GGTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACTCCGTCTCA
 AAAAAAAAAAATCAGATTGCTTTATTGCTGGTTTTCTTTCTAAAACCTGA
 GATTGGTCCCATCATCCCCTGGCCCCATTGGTTAATGGTTCTCTCTTT
 GTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGGTTGAATGT
 AGACACTGCAGGGTCTTCTGACTCAAAATGAGTAAGGCTTAGATAAAAC
 ACATTTTGAAATGCATTTCTGGATGAACAGCAAGGAAAGGAGATCTCTTA
 AAATCCTCTTTCTGTTCCCCTCTCCCTACCCCTCCAAGTGGGCTTAAGT
 AGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCCTC
 TCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTTTAAT
 TATGTGCCAGTGGCAAGAGCGGTGCTGAACCCAGGGGCCTGCCTCAATC
 CGGGGCTTTGAGGCAGAAATAAGTGGTCTCAGGTTGTTGGCATTTCCTT
 GCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTCCCA
 ATTGAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA
 CAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAGTGAC

FIG. 3 (38 of 52)

GTGAATGAGAATAAACACAAACAATAACCACCAGCTGGGATGCTCTAAG.
CTTCAGCTGTTAGAAATTCCTGAATATAGAATAAACTGCCACAATGGCAA
ACATGCACTCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCACATT
GTGCCAGATACCGACTCAGCTTCACACTCACCTCTCTACTGTGCCCTCTT
AATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTGTTCT
TGGCTGTGCTCTGGGCAGCACATGCAAAATGGGCAGTAACAGTGGCAGTC
ACAGGTAAGTAGCCTTCTCACAGTGTGGAGTTAAAGGCATGGGACTGAGA
CGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAGATGACCAGGGGCTACT
GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCTCTGCA
GGTGCAGTAGCAGCTTCTGTAGTTCCTGATCTCTGGGTCCCACAATCTT
CCCCGTTTTTGTCTCTCCACTTCTAATTTTGTAACTGACTTCCCTGTGTG
TACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCTTGATAA
GACATTGTCTGGTACGAACACAGTAACCTATTAAATCCGATATCTCTATG
AAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAGCAGA
GAAATAAAGTCAATTTGTCTAAGGTTGCACATTTAGTCAAGGGAAGGGTTG
ATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCATAAT
TTAAAAATAAACTAGGCAGGTTTAAAAAAATGAAGTAATCTATAAGTAA
AAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATAGCTG
AAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAATTCAG
CATAGATAGAAAAATGGGAATTTACAAAAGTACACAGGAATTATAAAAG
AGGTTAAATATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAACTGG
AATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAAAGAG
GTGGCTGAGAAATTTTTCAGAACCAACACAACTATGACTTTACCAGTAGA
GAAAACAATGTACACTGAGGAGGATAAATAAATATACTATGAACAAATTG
TAATAATAATACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAAA
AAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAACAAC
AACAAATGGAATCCAAATTCGGTCAAACAGTATTTCTTCATGCTAGCATA
TAGC

>Contig40

GGGAGTCCGCTATGCTCCTAAAGATTTGCACCTCTGATCTGGTTTGTAGT
TAGTCTCTTTTATTGCTTTATCCTACTCAACTAATTTTTTTAGTGCCTGT
TTTTTTTTTTTTTAATGTGTGTTGATGACTACAATTTCTAAACTCATTCTA
CTGATTCTATGGGTGCTTTAAATCTGAGCAGTCTTTCGCATTTACTGCCT
GTGATGGCCCATCCCAAGGAGATGCGCCCAAGTCTTCTAGGAGCAG
ATGTGATAACGAGTAAGGGAGAGATGCGCCCAAGTCTTCTAGGAGCAG
CCAGTAGGACCTTCCAGGGGTTGCAAGCAAACACAGCAATATGTGGAGT
GTGGCAGAGGATGGCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG
CTTAGTCTCTAGAGGAAATGCTGGAGAGGAGAGCCAGTCTGTACAGGCAT
GACAGCCCAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG
CTATCTCATTCAGAAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATT
GTACCCCAAGGAATTGCTAACCTACTTGCATCTGAATGATGTCCATCACT
CCCTTCATCACCTCCTCTGGGGGCTCTGCAAGGATTTGACTCCTGCATTA
GTGATCTGTCTCACCTACGTTGTGATTACATGAACCTACTAATGTGCTA
TGTGACAACCTACCATCTTAAACACAAAAACCTCTTTTGATTCTGTGGCT
CCCTCCAGCTACCCCTGCATTTCTCTGTCCCCCTGCCCCGTCTCTGCACT
CACTTTTATTTTACAGCAAACTACTCAAGGGAGTCTCAGTGCTCCTTGG
CTCCATGTCTCCACCTTTTCACTCTCTCTCAGTTCCTCTGTGAGGCTT
CCGTCTCTCAAGCTCTTCTTCACTTTTGTCTAGGGCCGCTGACATCCTCT
TTCTTGCCAAATTCAGTGGCCAGGTCCTCACTTACTCAACTGCTCAGCAT
TGTTGGGCTGGTGGACCACATTCTCCTTCAACCACTTTTGCTGCTCTC
TCTTCTCTCCAGATGTTTCTCTCTTCTCACTGGCTACTCCTCTTTTGTCT
CCTTTGTAGCTCCATTTCTTCTTCTTCAACCTCACTGTGCTGGTGTGCCC
AGTGCTCAGTTTTTAGCTATTCTCTCTTTTCCAGTGGCATTATTAGATG
GTATCATGTGACCATGGCATTATATGCCTTCTACATGACAGTTACTCCT
GAATATGAATCTCAGGAAAGATTTGGATTTATTTTTAATTAATTTTTTA
AATTTTATTTAATAAATGAGGTCTCTCTCTGTCTATCCAGGCTGGAGTGT
AGTATTGAGTGATGTGATTATAGCTCACTGCAGCCTTGAACCATGGGCTC
AGTGATCCTCTGCTCAGCTTCTGAGTAGCTGGGACTACAGGCATGT
GCCACCATGCTGGATGACTTTTGTGTGTGTGTGTGTGTGTGGAGACAG
GGTCTTGTCTATTGCCCAGGCTGATCAAACTCTTGGCCTCAAGTGAT

FIG. 3 (39 of 52)

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CCTCTCACCTCAGCCTTCAAAGTGCTGGGATTACAGGTGTGAGACCA
CTGGGCTAAGATTGAGATTTGTATTCAATTGACTGTTTGACATCTTCAC
TTGGACACCTAAGAGGTATCTCAAATATTAATTAACCTGGCCAAAATACA
GAACCTTTTGACCCCTGCCCCCACAATACTGCCCCCTCCCCAGACTTCTC
CATTTCTGTAAATATCCCCAGTTACTCAACCTCAAACCTATGAATGCC
CTTTGATTTCTTTCTTCCCTCATCTCCTACGTTGACGCCATCAGCTAGT
TTTGTGSCCTTTATGCCCAGAATATAATCCTCACCACCTTCTCTCCTATT
GCCCGAGTATAAGATGTGAGTTTTCTGACAGTCCATTGCCCTGACCT
CCTGAGTGGTTTGCTTCCACTTTTGACATTTGTATTCTCTTTCCCCCAG
GGTCAATTTTTCACAGCAAGAGTGGCATTCTTTTCTTTTCTTTTCTTTT
AGACGGAGTCTCGCTCTGTGCGCCAGGCCGGACTGCGGACTGCAGTGGCG
CAATCTCGGCTCACTGCAAGCTCCGCCCTCCCGGGTTACGCCATTCTCCT
GCCTCAGCCTCCCGAGTAGCTGGGAATACAGGCGCCCGCCACCGCGCCCG
GCTAATTTTGTATTTTAGTAGAGACGGGGTTTACCTTGTAGCCAG
GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCTCGGCCCTCCAAA
GTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAAGAGTGGCATT
TTAAACCATATATTAGATCATTGCTTTTGTGTTTGGGAACCTCCAAGGG
CTTTGCATCATATATCAAGTTGACACCTCTCCTACCCAAGCCTGGCTCTT
TCCTGCTCCTCTGTCTCTCAGCCCCCTCCACCCATTGTTGCTGCTGCTC
AGCCACACTGGCCTTCTTGCCATGCCACATTTGTGCTAAGCCCATCCA
ATCTCGGGGCTTTGCACTCGCATTCTCTGCTTGGCATGCTGTACCCC
AGATCTTTCATGATTGGCAGCTTCTGTACATTACGCCACCTGCTCAAGCC
ACCTTTTCAGAGGGCCTTCCCTGGCCACCTCACCTGAAATAGCACCTCCG
ATTGCACCCATCCGGTTATTCTCCATCCTGTTCTCTTGGTGGTATT
CCATCACTGATGAGGAAATGAACCATGGAATGCTAGGGCTGATGACCAGA
ACTTTCCCCCACCCTTATTATTACAGAGGAGGAAATGAGGTGCGAGGT
AAGATGGGCCCAGGATTTCTACTCCCGCTGGACTGCAGGCCACAGCACTG
ACCTCAGCTGTGCTCACTCTTGGCATTACCCCAACCTTCTATCTCCAAC
TGCCCCATTTACCAGAAAGTGAATGTTCTCAGAGACGGTGAGCCACCTG
ACTTGGACAGCAGCCAGGGCCCCCTGGCACCTGCTTTCTCTCCTGCTG
CATCTTTCTCTCCAAGACCTACCTTTCCCTGTGATTCTTGCCACATG
CTGCATTTGATGGTTTATGACCTGATTTCTGAGAGGATTGAAATTTT
ATGATTATTTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA
GTGCTTCTGGACTTCCAGGGACAAAATCTTGTCACTTGGCTTGGCTTCA
TATTGCTAATTAAGGACCCAGGATGTGGGTGAGATGTGCTAAAAGCTGAG
AGGAGGCTCTGGACTCTGACTATGGGCCCCACACCTTGGGCGAGGCATCAC
ACTAGTCTTTAGTCACTCTCAACCCAGCTTCCAGTTGAATCAGATGTT
TGTGAATAACTCAGCAAGGCTGTATGGGAAATGAAGAATGAGGTGGGGAA
GAGGCTCTGAGCAAGACACACTGACTTACCCCTTACCTCTAAGTAGGG
TGTGTAGCAGCCACCCACCAAGTCTGTCTTCCAGACCACGTATGC
TTTCTCCACCTTTGATCTTTTATCTTCTGCCAGCCAGATGCTTGCTG
ACTCCAGCCCCAAGCCTATAGGATAAGCTACAGCCTGCTTCTACAGACTAC
GCATTGACAGATCTAAGACATCAAGTCAAGTTCGGAAGCACTTGCTTCT
CCTCTCCAGGTACACAGGCTCTCCTGGAAAGCTGGTAGCAGCTGTGGAGG
TGTGGTGTGTTACCTGCTGCAGGTGCAGAGAAGTTGACTTACAGCCCTT
CAGAAAGACTGCCTTCTTCCAGTTGTATTTGTGTACTTGTGTTGGGTGTGG
GGAGGATTCTCAGCTTTCTCACTCAAATTATCAGACCTTTCCATTTAG
TGGTAGACCATTTCCCTCGTCCAGGCCAAGGGCAGATAGTACAGAGAAAT
AGGGAGTTGTTACCCAGGGAGAGAACTTGGCTCTAAACCTGTAATAGAAA
GGTCAGTTCTGGTCTGGAGGGTCAATTTTGATCTTGGCTCAGATCCAGG
AATTGGAACCAAGGCTTTTGAACATTTAATGCAGGGGATTAAAAAATG
ATACGAGTCACTACGAATATATTTGCTTAACATCTAAAGAGATCCCTCA
AAACACTAGAAAAAATAAGAACAAAAATCTAATAAAACAAAATTTGTTAA
ACACATTTACCAATTTTTTTTTTTGGTAAAAATCAAATGTCATAAATA
AAGCTAAAGTTCCTCTTGATGACTCGCTCCTCTGCCCTATTCCACTCCAA
GTAACCACTATTATCAGTCTTGCCAATACCTTCCAGACCTCTCTACCTC
TATATACCATTAGAAGCAGATGGTCTTGCATTGAGGATGTGCAGTGTCTT
GTTTTACGTAAATGTTATCACTCTGTTCTTGTTCATAATTTGCCTTTTT
CTCTCAATGATTGCTTGGCTATCTTCTATTTAGTAGCATCTCCTTTC
TTTTTAACCTTACCATTTGTTTATTTAACCTTGCCTCTATCAACAGATATGT

FIG. 3 (40 of 52)

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AGGTTTCTTTCTAGTTGA. TTCATTAAGTATTTATAAAACAACGCATCAG1A
ZATGTCCATAAATTTCTTTACGGAGATGGCAAGTAGTGGAATTGCTGAG
CCAAAGAACATGTTTAAAAAACCCAAAAAACTAGACGCTACCAATTTTC
TCTCCAAAATGGCCATACCCACTTACCCATACAGAGATGATTTGGAATCT
GGCTTCTCACAAGGTGAGATGCCTTCACAGTTTCATTCTTCCTGGCATG
TCTTCCCTTTTGTATCTGAGAGAGCTGGCAGAATTGTGTCACTAAATCAA
GGATAGAGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTTCTT
CCCAGACCACCTGCTTTCTGCCACCAGCTCTGTTCCATCTTATAGAATG
GTTGCCACTTGGGTGTCTGCTCCGACAGCCATGTCATCCTTTGCACTGCA
GTTATGAAGCAGACAGAGCTAGGAGAGGGGCTTTGCCAGCCTCTGCCCTA
GCTTGGAGAATTTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCGAAGAC
TGGCAGCTCCCTCAACTCAACAGTTGTCTTCCACAAGAAGTCAGATACA
TTTTTTTGGGATAAAATATTTAAAAATTATTTATTTTATTTCTGAATAATA
TATTTTACATGATTTCAAAAATCAAACTGTAGGCCAGGCATGGCTGCTTATG
CCTGTAATCCTAGCAATTTAGGAGGCCGAGGCGGGAGGATCACTTCAGCC
CAGGAGTTCAAGACCAGCCTGGGTAACATAGTGAGACCCTGTATCTACAA
AAATTTAAAAACAAAATTAGTTGGGCATGGTGGCTGATATGGTTTGGCT
CTGTGACCCAACTCAAACTCATGTTGAATTTAATCCTCAATGTTGAGG
GAGGGTCTGGTGGGAGGTGATTGGATCATGGGGTGGGTCTCCCTTGC
TGTCTCATGATAGTGAGTGAGTTCTCACAAGACCTGGTTATTTGAAAGT
GTGTAGCACCTCCCTTCACTCTCTCACTCTCTGCTCCGCCATAGTAA
GATGTGTGTGTTTCCCTTTGCTTCCGCCATGATTGTAAGTTTCTTGAA
CCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAGCTGTGAATCAGTTAG
ACCTCTTTCTTCTATAAATTACCCAGTCTCAGGTCATTCTTTATAGCAGT
GTGAGAGTGGATGAATATAGTGCCATATGTTTGTATTCCAGCTACCCAG
GAGGCTGAGGTAAAGAGGATTGCTTGAGCCTGGGAGTTTAAAGGCTGCAGTG
AGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGACAGCGAGACCTTGT
CTCCAAAAAATAAAACCCAACTGTGTAAATGTGTTTATAAAAGTGTCT
TTGCTCCACACCTGTCCCTATATATCTTATTCCTCAGCCTCCGACAACT
ACTTTTATTCATTTCTTATGTATCTTCCAGAATCAAAAAAATAATCAA
TACAAGCACAGTGAATGTATTGCCCTTCTTCCCTCCCTTTTGTTACAT
CAGAGTTAGCATATCATAAATACGGTCTGCATTTTCTTCTTTTTCAGCTA
TCAGTCATGTTTTGGAGAGGATTTTCAATTCGTGCAGACAGCATGTATTAG
TCAGTCTTGCATTGCTATAAGGAAATACCTGAGACTGCATAATTTATAA
AGAAAAGAGGTTTTAATTGGCTCACAGCTTCGAGGCTGTTCCACAGGAAG
CATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAGCTTTTACTCATGCA
GAAGACAAAGCGGGAGTGGATGTCTTATATGGCAGGAGCAGGACTGAGAG
AGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTTAAACAACAGATCT
TGTGGGAACCTCTGTACGAGAACAGCACCAAGGGATAGTGCTAAACCAT
TCATAAGAACTCCACCCCATGATCCAATCACCCACACCCAGGCCCCACC
TCCAACATCGGGGATTACAATTTGACATGAGATTTGGGCTGGGACACAGA
ACCAAACAATACCAGAGTGCTTTCTCATTCTTTTCTATAGCTGCCTAGTA
TTCTATGTCTTTACTTCATTTAGGCAGTCTCTTGTGATAGACACTTGG
GTTACTTCCAATTTTTCTTATTACAAATGATGTGCAATGAATAATTTTGA
TCATTTTCCATTTTACATGGGTTATGTCCATCTGTGGGATAAATCTCCAG
GAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTTATAGTT
AGCAAATTTTGTCTATAAGGGTCATATCAATTTATAGTCCACGCGTAA
TATTTAACAGTGGGGATTTCCCGACAGTTTGACCAACAAGGTCTGTTGTT
AAACTTTTGAATTTTGTCAATCTGATGGGAAAATACTAGTATCTCAAAGT
GCTTTTAAATTTGACTTTCTTATTACAATGTTAAGCATCATTTTACTCTGC
CCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGACTGTTAAGATCCCT
TGCCCTCTGTTTTGCTGGATTTTTGTTCTTTTTTTTCAAATGTTTTGAGG
CAGTTCTTTACATGTGAAACAAGTTATCTCTTTATCTGGGGTGTGAGTTA
CAACTACTTTTCTCTGGCTTGTGTTGCGCTTTGACTTTGCTTCTGGTGA
TTCCCGCAATTTCTGAAAGTGTAATTTTGCATCATTCATTCTTATACACC
CATGCTCTTGTTCACGCTGGTTCCTCTACCTGAGGGCTTTTCTTTTCTG
CTTCTATCTGGGAACATTTTTTTGAGAGAGAGTCTCACTCTCTCGCCAG
GCTGGAGTAGTGCAATGGCGGATCTTAGCTCACTGCAACCTCCACCTCC
TGGGTTCAAGCAATTTCTCTGCTCAGCCTCCCAAGTAGCTGGGATTACA
GGAGCCCAACCAAGCCAGCTAATTTGTTGATTTATTTATTTATTTT

FIG. 3 (41 of 52)

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TGTAGAGATGGGAGTC...ACTATGTTGGCCAGGCTGGTCTTGAAGTCC...
GGCTCAAGCGATCCACCCACCTCGGCCACCCAAAGTGCTGGGATTACAGG
CCTAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTGTTTATCCCTT
TAGGCTTGATTCTTATGTCTTCTCTCCCTCCTTCTGGATACTCCTCT
TGTCTCTTATCTTACTCTACTTGTCTATGTTACCTTGTCTGCTTATAAC
TAGCTCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTCTCATCTCTGT
ACTCCAGCTCCTAGTACATAGCGCTTGGCTCAACAGATGTTTGGTGCAAT
GATAGATAAATCACTGGTAGCTGTTACTACCAGTCTGACTCCTGTCAGT
GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTTCTGTTGAAC
AACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCCGGTGGCCAAGGA
TATTTTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGGGCTTTAGTCC
CCCAAGAACTCTCACAGCCCTGGGTGCTTTTACTGTTTCACTGTCAGTGTCAAATCC
AAGACAAGTCAATGATCAGGAAAGACCAATTTTTTTTGTTCAGTGAAGTT
TATTTTCAGAATCATTGAACAGTATGATATTTGGTAATTTTATAAATATTC
CCACTTAAAATGATCGGAGCAGATATATTTTCACTCGTAATTAAGGACA
TGATTTAAAGAGAGCACACCAGTCCAAATTGAAATGATTCCATAGCTATT
AAAAAACTAGGGTTTTTACAGACAATGATACTTTTGGCCCCCTTTGAAT
AGATTAGACCAATGAATAAAACAAACAAATAAATAAATAAATAGGG
AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTTCTTAGA
ACCAATGTGGCCGTGGTTTTCTGTGAGGCGTCTTAAGTGAGTAGGAGA
GGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGTCCCTGAAGAA
CCAGAGCTGANTTNCATCAGGAGTAACANAGGTAGATAG
>Cont: 341
CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCCAATTATCAACATTAA
TGCACATTTTCAATAGAACCTGTTCCGGCTTTTCTTAGGAGGGGGGGGGG
GAGACGTTGTTCTCTGGGAATAAGTGTAACGAGGAGGCTGAGAAGGCTTC
ATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTATCATCTTT
CAACACGCAGGACAGGTACAGATTTTTTCTTTGAGGCCCAAGGCCACAG
GTATTTTGTCACTTTTCTTCTCTTGTACAAAGGACATGGAGAACACC
ACTGAAGAAAGAGGGGGTCTTGTGGTTAGGGACACAGCAGTGCAGGGTC
ACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTGGTAGCCTC
TGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGATAACTTGA
CTTCTCACAGACAATAGCAGGGTCATTTTGTGATTTAGGGTTTCCCTC
AAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACGGAGAATGA
AAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGCCATTG
TGTCACTGGCTGGCAATGTGCCATCCACAGGAGCGGAACAACTTGATCA
ATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAGAAATCAGG
CACCAGAACTGTTTCAAGAACAGAGAGTAGCCCATGGGAAGAAACTGGGA
GAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACACTCATTTT
ATCTTCTCAGTCACAGCAGTGTCAATTGGAGGCCCTGGGATCACTCTTA
CTACCCGATTTCAAAGAAACAGGATTTTCTTGGCCTGGCTGAGAGCAAAT
AGCTTCCCCCTGAGTGAGGCTGTCTTCAAAGTCAGCAGCCTTAGTTGCC
CACACTCTGTGTCAGAGGCTTTGGCTACTGTGGCAGGATGCCAGGCAGAT
CACCACAGCTAATGATGGGTTTACCAGCACTTGAACTTTTGGCCGTTACA
GCGGAGAGATATAAGTTCTGTGCTGGGCGGTAAATTTCCCTACAAGGAAC
CACCTGGCATTTGGGTGGGACGGATGTTGGGGCAAGGGGGGAAGACTGGGG
AGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTCAGCCTCAACAA
CAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATCAAATGACCCC
ATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGACTTGGGTGGAC
ATGGTCTTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGTCACACTCCTG
TTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTTCTAGGACCAA
AGTTTGTATATCTTTTTTAATATTTTTTTTCACTTGTGTTGATCATTTG
CCTTAAATTAACTTTCTACTTTGTTTAAACATGGAGAATTAGCAAGCTG
CCAGGAGGCCAGGCAGGGAAACCAGGATGTTTCCATTTACCTTGTGTGCTC
CATATCTGTCTCTGGAGGTGGAGAGCTTTCACTTATATGGACCAAGACA
TCACCAAGCTTTTGTGCTGTGAGTCCCGAGCGTGTCAGTTTCACTGATCGT
ACAGGTGCATCGTGCACATAAGCTTCGTTATCCCATGTGTGGAAGAAGAT
AGGTTCTTAAATGTGGAGCACATGTTGTTTAGGTATAAAATCAGAAGGC
AGGCTCTGTGAGGCGAGGTGGCAAAATTTGATTTCTTGGAGGACACCTGA
GCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGATGAAGCTGGGA

FIG. 3 (42 of 52)

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GTGGGGTGGCTAAGAAL CTGGACCTGACACTATTAGACATGGGTTCC...
CTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT
AAAATGGTGATGGTCATAACACTAGCCCAAGGGAGGTTACGAACCTCTG
GTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGGAGTTGCAAAT
GTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCACTAAAGAGATG
ATTGCTTTGGTTTCCAGCCTTCTTTGTTTTGTCTCCCGCTGGGCTTCT
ACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCTGGGGCTTGAT
GACTTCCAAGAGGACACAAGTGGAGATCTACTGCTGCTCTTGGCTAACT
ACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCAATTCTCCTGGA
AGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTCCATGGCCACA
ACAACCTGACGCGGCTGCTGAAGCCCTTGCTGTAGTGGTGGTGGGAGAT
TCGTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCAGGTCTGGAAGG
AGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTGGTCTGCCAG
GAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAGGAGGAAAGGG
CTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTGGGCCAGGCGT
GGTGGCTCATGCTGTAAATCCAGCACTTTGGGAAGCCGAGGTGGATGAA
TCATTTAGGTCAGGACTTCAAACCAGCCTGGCCAACTGGCGAAACCCC
TTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGGGTGCACCTGT
AATCTTAGCTATTTCAGGAGACTGAGGAAGGAGAATCGCTTGAACCTAGGA
GGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTCCAGCCTGGGC
AACAGAGTGAGACTCTGTCTCATAAAACAAAACAAAACAAAACAA
AATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAAGCTCAAGGAG
GTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCAGACTCAAGAT
TAGAATGTGGGCTTTCTGACACCTTACAGGCTATTCTTTTAGAATAAATC
CCATTTCTACTTTGTTTCATCTTTTGTACATGCCCCACCTACACCATAC
ATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTGTACACTATG
ATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATTACCTATGCTC
ACTCAGCAAGTATTCAATTTTTCTACACTGTTCTTTTTTTCTTTTTTCA
TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTTTGTG
AAATGTTACCACTTCTCTTATTTCAGAGAAGCTCCGTATTAAGGCTTCA
CTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTGAAAGACAGTT
AAAGAGACCTGTAAAGTGACAAAAAGAAAGTTGAGCAGGAGAGAATTTCT
GCCTGGAGCAGAGCCAAGCTGCTGGAAGAGGCAATGGGGGCAAAGGCCAG
GCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAACAAGTTATGCC
AGTCTTAAACCTTCTAAAGAAATATGTTTTAACAAGATTGAGGACTGGA
TTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAATAAGCCAGAG
AAAAGTTGGCTGCTTCCAACCTGCACAACTGACCTAGCTAGGCTGATGGC
TGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC
AGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAAATGACCATT
GCTGCCCAAATGCCCTTAGCTACAACCTGAAAAATTTTCAAGACTGGAGGT
TGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCCTTTATTTTTT
AGATGAGGTCCAAAGCGGGTAAATGACTTGTCAAGGTCAAACAGCAAGT
GAATGGTTTTCTTCAAGTCTCAATTCATCTTTTGTATATCATCTAT
GTCTTGTGTATAAGCTTCAACCCAGGTAGCAAAAACTATTCTACTCA
AAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTGGTTTTAGAGT
TTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAAAGGATAATC
AAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAATGGGAAACAT
TATCACTACTCTCCCTGTCCACCACCAAGTGTGGCCACCACCACCAACG
TTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAGGTGAGCAAGT
GGTGAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTCTAAAAACAAA
TACCATGGCATCAAAGTGGCCAGAACTCCCTTCTTTGAGCTTTCCCTGT
GTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTCTTACCTTCAT
CTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCCTCATTGCCACTGT
AATAAAACAGGGACATGTCTCAATTATGTCTTCTAAACAGGTTTATTTT
TCCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACTGCAACAGCC
TGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTACAGTGATATGCG
CAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGGGCACCCTGGG
TGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCAGCAGAGTCAGCT
AAAACTCAGCTCTCCCTCTCCCTCCAAGCCACACTTTGCAAAGGGATTCT
CTTGTATTGTGGGCTTGAATCTTTTCTCCCATTTGCTCTGCAGGAAG

FIG. 3 (43 of 52)

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CCCTTGCACAACACA TGGATAGCCTCCAGGTCCCAAGGCTGGAGC
CTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGGCACCCTGTTT
GCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCCAAGCACAGAT
AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGTCTCAGCG
TCTCCACTGACCTGTAATAAGCCATCATTTCAGTGGCGAGCTCAGGTACT
TCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAAAAAGAGTGAC
TTCCCCATGACGGCTACGTTTATGTGTGATTCTCTCAGCATCCAGTGCA
TGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATGAATGTGTGAA
AGAGAAGTCCTTTGGGTCTAGAGAAAAGCATTGTCTAAACCAAACCCAA
CTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTTGACACTAACC
TTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCAGAAATATTTCC
CGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAAAAGCTGAGAG
AGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAGAAAGAGAGAG
AGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACAGAGAGACTCC
CTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA
TTGGCTGAAGAGAAATCCAGAGCAGCCTGTTGTGCCTTGTGCCTCGAAGA
GGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTTATAGCTTTCAAAAG
CAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTGATTTCACAAT
CAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGGAAGCTTCTTAGGGGAG
GGGACTAATAAACTGAGATAATTCTCTGGTTCATGGAAGGGCAAGGAGTA
GCAAACTATGACACATTTTGCAATGTATCACCATGCAAAATATGCATTGT
TTTCCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAATACTGGATTT
TCCCCAGTTAGAAGAATGTTTAAATTTAGTATATGTGGGACAAAGTGGAA
GACACACAGATTTATACATGCACATACTTTTCTTCATTCACTTCTTTGTA
CTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATGGGTACAATGA
AGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGTCTCTACCTTG
GGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAGGAGCCTCTGA
GGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATACGGTATGCAGG
GTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAAGCTCACACAA
CCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATGGATGAACCAG
ATCAATGCCAGATGAGCTCTGCCTAAATGATTTTTTGGTGAACTCTGAA
AAGTGGAATATTGTTTCTGTAAGAATATCCATCTGAGACTCTATCTCTTG
GTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACACCAGCAAAGTG
CCTGCTCCAGGGTAATGCCAGGGGAGCCCTCCATTTGTAGAATGAATGA
GAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACCCTCCTTTGCC
TCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTTGAGACAGAG
TCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCAGCATCTCGGCCCCCT
GCAAGTTCCGCCTCCGGGTTACACCACTTCTCCTGCCTCAGCCTCCCCA
GCAGCTGGGACTACAGGCACCTGCCGCCACGCCCCGGCTAATTTTTGTAT
TTTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGGTCTCGATCTC
CTGACCTTGTGATCTGCCCGCCTCGGCCTCCCAAAGTGTGTTGGGATTACAG
GCGTGAGCCACCGTGTCCAGCCTGTAAACACTTCTTATAGCACTGAGTTGA
AACCTTGCTCCTCCTGGTTCCTCCAGGAACTGAAATCTTTTGAGCCAA
GTCTAGCACAGTGCCTGGCATGTACATTCAAGTGGTAGAGTTTGCTGCTT
GAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAATTAGTATGTGC
CAGGTATCGTGTCTCGCTCTGCATTATCCAAGGGAGTGAGCCTCTGTGCAA
GTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAAAAGAGCATT
CATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTAAATTTGGCTCCCAGT
ATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTAGTAAGTTATA
TTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTTTCTCTGTAAT
TTGATAAGCCATAATCCATTCCCTAACACTGAGCCCTCCTGAAATTTGGTG
TCTGGTCTGTCAGATAGCTAAAAGCCCTGTCTGGGTGGCCTAGGGACTCC
TCTGTTTTGCTCCACAGGATCCACTTTGCAAAATTAACCACTGGTTCTCC
CGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTCTTCTCTCTCTC
CTTCT
CTTCT
TCT
CT
CT
CT

FIG. 3 (44 of 52)

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TCTACCTTTTATCCCCGCTGGAGTGCAGTGGTACAATCATGCATTCA
TGCATGATCACAGCAGCCTCAAACCCCTTCTCAGAGTCTTTATGCGGCAA
CCAGCAGGGTCTGGAGGGTTGGTGGCTCTGTGAAGTCTCCTGACAGAACA
CAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGAACGAAGGAAGA
TCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCCGAGCATCAGCT
CTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAGGTGAGAAACCT
TGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAGGACCTCAGAAT
CTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGATATGGTGGGAC
CACAGAGATGAAGACATGAATAGCTATTTGAATGTGAACAGCAGACGAAG
AAATCAAGGCTAGGAGGGTGGAAAGTGACTCATCCAATAGCACAGTGTGGT
TGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCCGTATGCTTTTCGCTCG
AGGGAAATTTTGGAGCCATGGGGCAATGCCCCCTGACGTAACAGTCTCCA
CAGTTCTGCCATGTCTCATCTTGGCCCTGTAACCTGGACCCAAATCTGCT
ACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTCAAATAGGTTGT
GCAACGTATGTATCAGATCCTGTCTTCCAAGGAGACCGCTCAGGCCACA
GCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCGCTATAAACATA
GTTGGCACTAAGGGAGGGAGTGAAGAGTGATGATGATGTAGATGGTGTAT
GTAGCCCCAAGGAAGTGGAAACAAGCAGAGATGGGGAGCTGGAAATGCCAG
GATGCTCCAGCTTTTGGGGAATTATTCAGCTCTTGAGTCACTAAAGCCTT
TCTCAGCTGCAAGTTCCTCTTTACCCTGTGAGGTCATTCTTCCAAGACAG
GAGACTGACATTTATTCAAAGCAGCAAGTGGCCTGATACCATCTTGTGTCT
TAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTCATCTCATTGGT
CTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCATGGGTTAGTTC
TTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTTGTAGTGAGCTG
TTCTCTCTTGTTCACCTCTTGTCTTAGAACAGAACTAAGCAATCTGCCC
CCAACATTTTCCCCAATTTCCCATCTCATTCTTGGCACTGGCTTCTTAAT
ATTTGTTCTTATGAGTCATTTTCTTGTATCATTTCCATGAGTCCCTCTGG
GATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCTGTCTTGTGGA
TATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGGGAATGGGCACT
ATGATTTTTATCATATCGCTTCCACTTCTTTATGGCATCATCTCCAATG
GGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGGGACATGCAGAG
TCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAAGGAGGGCTTAG
ATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGTCTCCAATGGCT
TTTCCCTGATGTGCGAGTTGTTATGTGAGTCTGGGAGACCAATAAGACC
TTGTCTCTCTTGGATCCATCAGAAAAAGCCCCCTGGGTGGGTAAGATGG
ATGGCAGGGCTCTCCTACTCTATGTCTTTCTCACACCTAGTGGGTATAA
GAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCATTATCCAGGGTCT
GGAAACATTTCTGTAAAGGGCCAGATAATAAATGTTTCAAGGTACAATA
CTCAACCTTGCATCTTTCAGAAAAGCAGTCAGATAATACATAAATGAAT
GGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATATCATTGTATTA
TATCATTTTTTCTTACATACAAATTTAGAAGCAATACTTAAAAAAAAAAAA
GCCGTCTTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTTTCCCTC
ATTATCTTATTAATCTTTCATAATAACCTTTAAAGTAGATAAATTTGAAC
CATTTGACCTATGCAGAACTGAGGTTGAGACAATAAATTTTAAAGACC
GCACAAACAGTAAATGCTGGAACACGACTCAAATATGGGTTAACTGAAC
CAAAACCAGATCTTTATTTCTCACTTTAATTGTTACATATGTTTATTGC
CTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCTTTCTCATTCTC
AGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAGATTACCTCTG
TCCCCATAATGTTTCCACATTGTCTTTTAGGATTGAGATCCTCTCTGTT
CCCTTGTCTTCCCTCCTTTCTTCTTGGCGGTGACGTGCTGTGTGAATT
TGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCAAATCAGGGTTT
TTAGTGATCTCTCTTCCCTTTTCTGAGTTTCTTCTTATTCCCATCACT
TTCTCATCTATAAGTGGCAGCTTTGTTGCTGGAGGATTTCTTTGTCTCT
TTATTCTCTTTAAGACTTTGTCTAACTGTCAAAGCAATCCCTTGAAG
GTATCTGTCTTGAATTGTGTGCTTATGATGCTGAAAAATACTCTCTTC
CTAAAGCTATTATAAATGCT
>Contig42
GGCTAGCTGCAACTCTTGAATACAAACACATTTCAGACATGCACACACTTT
CTGGCTCCCCAAAAGAAAAAATAATCAATTTATAATAATTCTGATCCT
TTGCTTATTTCCACAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

TTCTTAATATTCTCTT...TCTCTCATATCCATTTTCCTTACTGCTGTC...
CACCTATCTCTTCCAAACTCCCTGTTAAATCCCTGCCCCAGCGAACTTT
TATTCAATTTTGTGGAATGGAGGCTGCACTGATTTAAATTAATAAAAAA
AAAAATCCCTACTCCATGTCCCAGATCCCTAGTTGTTTTTGTGTTTTTG
TTTTCTGAGACAGGGTCTTGTGTCTTCCATGCTGGAGTGCAGTGGCATG
ATCATGGCTCACTGCAGCCTCAACCTCCTGGGCTCAAGTAATTCTCTTGC
CTCAGCCTCCCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGC
TAATTTTTCTTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAG
GCTGGTCTAGAACCCTGGGCGGACGTGATCCGCCTGCCTCGGCCTCCCA
AAGTGTGGGATTACAGGCGTGAGCCACTGCTCCCGGCTTGCGGTGCAAA
TTTGAGCTTTCTCACTTATTAGTGTAAAGACATACAGCTAATTTCTAAATC
TTCCAAACCTCAGATTTTTTCATCCATGAAGTGAGGATTATTATAGAGCTC
ACTAATAACATGGCTTCAAAAAATATATAATGCCAAATTGAGATCAAAAT
AATAAATCTATATTACATGGGAGATCTTAATGTACCTCTTATATTATTGA
TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC
ATTTAATCAATAGGACCAATACATTTTAAATCAATAGGATCCTCAGGAATA
TATACAGAATACCAAACCTAACAACCTGCAGAAAACATGCCAAACATTTAG
GTACAGACATTGTTGGAAAATGCAATCTTGAAACGAGTGGACTGACATTC
AGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAACCATGTCTTTA
CTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCACATAATTTCTTC
CACTTCTCTACTGTTTCTTGTCTGGGCTCTGTCTGCTTACTGTCTAAT
ATCTTGGCCCCCTTAAAGTTGCTAATCTTCCAAACCTCATTCTGTGACT
GGGCGCTGCTTCTTGTTCATGGGCTTGAAAATACTGACTGTACACTTA
TCTGGAGCATCCAGTGCCTTACCACCTGACCCAGATTCTCATTGCGCTCC
TCCCTCTCTCCACCTATTGGAATTTGCTCATACCGGTGTGAGACCCCTCC
TTTCCCCCATCTGAATTTTTATCAAGACAACGCACTGCCATACTCCCTC
GTACCCTGCTCTGGGCATCAGACTGAAATGTTTGTTCATTGAGGATCTG
CAGCTGCATCAGTTTCCCCAGCACCGTCCCAACCCCTTGAGCATGGCTAGT
CCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTATACATGCTGGGA
CAAATAATAAGAAATGACAGCATTTATGATAATGCAGGCTGCAGGAGGC
AGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCTCCAATCTTTG
AATATTGGACTATAGAATATGTCTATGGATCTATGCTCAGGTGGGTTCCCT
ATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTGTCCAAGAGGGA
GTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACTGGCCCACTT
GTGTGGAGACCTCCAGAGAACAGAACTCTGGGTTGGTGCCATGTACTTCCA
GGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGGG
CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCACAGGG
CTTCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCAAAAAAGGACAA
TTTTCTCTCTCTTTCATGAAGACTGAGCAGTTTTACCAGATTCCCAGG
GAAACACCTTCCACTCTGGGTTGAATGTGAGTGAGAGACATTCACTGG
AACACTAGAAAACTATTTCTGAGCCACTCACCTTTAGCCCTAGAAAGT
GTTGGATTGTCTCTTCTTGTGCCACAGTAGAGACTGCTGATAGCATCA
GAACCTGGGCTCTGGAATTAGACAGATATGGGTACAAATCTGAGCTCTCT
CACTTATTAGTGTGGGATGTAGAGCAACTTTTAAATCCTTCCAAACCTC
AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCACCTAATAGGG
GTTTTTGAGAATTAATAAAGTTATTCAATGACAGCATTTAGCAAGATGC
CTGACCATTGAGAAAATAACAAATGTTTATTATTATTGTTATTATTAAA
CATCTTCTGACCTTCTGACTGGGGCATCGTATCATCAGAAATACTT
AGGATGGGATGGATTCTGCTGAGTGGGCTGAGTCAAGGGTGCAATAATGGAG
GAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGAGCCAGCATGG
TACAAGGCTGAGCTAGTGTGCTGAGAGCCTCCTTGAACAGCCACAGAGCT
TGATCTGGCCCTGGGAGGAACCTCTTCTAGCTGGCAGGACCAGCCACAA
CAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTAGGAGTTCAATTTGGA
CCAAGCCTGCTTGGAGAGGGTTATAACAGGGATCCTTCCCTACTGGCAG
GTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTGATGGAAGGTGG
AAGGCCCTGTGCTGGGCCAGTACTATCAGGGATGGGCGGGTGGCTGGAA
AATAGCAAATAAGACAATATGATAACACAGTTAACCACCACACTATGTGA
AGCTACAATATGGGTATCTGTAATAGACAATTCCAATGTAGAGAATAATT
CTAAGGTGTCTCTCCCGCCAATGCCATAAGCACACGGCCTCTGCCTG
GGTTCTCACTGTGGAATGTCTCTCTGCTCTCTCATGCCAGAGAGTGG

FIG. 3 (46 of 52)

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GAAGTACTCTCTACTTT. .CACC GGCTTTCTGTCTCTCTCTGCAGCC...
CCTCAGCCCCCTCTGCACAGGGAGGTTTCTCTCTCTGCTGCTGCAGTGCTT
TGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTCTTGTCTCACC
ACCCTACATCACTGTAAGCTCCCAGGAGCAGGCTTCTGTTTGACTCAC
CTGTGATCCTCCACCTCCACCCCTGTAGTGCCTCAAGCATTGAGGACAAT
CACTGGCTGCCCCCTTAACCCAGAAATGCTGCCGAGACAGGAGGCCATGGC
CCAAGTTCCTGGAATGGGGTATTACTATGTCTCAGCACAAAGGCCTTTGCAC
AAATGAAGGCTTTAAAAATGCAGTCTTAGTCAGGTGGAGGAGGGCTTATA
GGATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCTCTTGTCTCTG
TTAAACTCACATCCTACGGCCCCAAATAACAACAAAAAATGGATGTAAAT
TCTTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGC
CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGA
GGATGGCCAGTGAACCTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGA
GCAGCAGCCTCGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTG
GGCAGGCTCGGTGTCTGATGAAGGGAAATGCCTGGCAGCACGTGCTGTCT
GTCTCTCGTGTCACTTACCTGGCTTTGCTGCCAAGAGGCCACTCGCAT
TTCTCAATTTTTTATATTTTTTTAATTTTTTAAATTTTTTATTTATTTT
TATTTTATTTATTTATTTATTTTAAATTTTTTTTTAATTTTTTAAATTA
TGCTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTAGTTACATAC
GCATACATGCCCATGTCTGGTGCCTGCACCCACTAACTCGTCTCTAGC
ATTAGGTATATCTCCAGTGCTATCCCTCCCCCTCCCCCACCACAA
CAGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTG
AATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTTCAAAAT
ATCAAAAGAGTATCCTTGGGAATGACTGGAATCCAGAGTCTCTGGTAA
TCCTCATAAACAACCTCCTGGATGTCTCTCAGCACATCTCCACCTGAA
CGCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCCTTTTTTT
TTTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCTGTAAATAAATCA
ACTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAA
GGAACCAAAGGCTTTTCTCCCCGCCCAACACACATAACACACACACAA
AATCATAAAAACATACATACCCCCAACACATAACAACACACACACAC
ACAAAAATATATACACACACACACCAAAACATGCCACAAACCTGTGT
CAGAGATAGATCCTACTGGTGGGTTTGTGGTCTCGCTGACTTCAAGAATG
AAGCCGTGGACCTTCGCAGTGAGTGTACAGCTCTTAAAGATGGCATGGA
TCCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAA
GCTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGC
CAGCTTTTACTTCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCA
GAGTGGCCTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTG
CTGATTGGTGCATTTTACAGAGTGTGATTGGTGGCTTTTACAATCCCT
TGTAAGACAGAAAAGTTCTGATTGGTGTGTTTACAATCCTCTGTAAAG
ACAGAAAAGTTCCCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGCCT
CACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACAT
ACATACACAAAGTATACATGCATCTCCCCAAATATACATACACAGAA
ACATACACACAGGAACCTCAGCTACCTGTCAAAGTCTGCATGGTATTGC
CTCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAG
TCCTTAAAAATCGTTGTAAGATAGAAAATTTTTAAAAGTATATAAAATAA
AATATGTATGTCTTTGGTCTAGCATTTACACATGTAGGAATTTATCCTA
GTGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCAC
AGAAATTATGTATGCATATGTGTGTATATATATATATCTCATACATA
TAATAATGTAAAAGTGAAAAATACTCAGATGTTCAAAATTGAGGATTAGT
TAGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTC
TCTCGAGCTTCAACCTCCTATAAACAGTGTCCCTGTATATCAGTATTGG
TACAGATAATCGAACTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGA
GTTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAA
ACTCTTCTCTCTCATTTCCTTCCCTTCCGGAACCACTTGGTTGAATCTC
TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCC
ATCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCCACTCACATCCT
CATTCAATCCAGAAGTGAGCAACACAGAAGTGCTACAGTTACCCCAACC
ACCTTCTTAGAAGATAAGTTAGTGTGTTTGTGTTTAAATTTTTTA
CTTCTCTTTCTTCACAATCTCATCCCATCCCAAGAGGTTTATCAAGA
AGTTCTCTAAAGATATGTGTCTCTTATGGAATTTAACAGAAATCAGGGA

FIG. 3 (47 of 52)

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...GAAATCAGCCATCAGGGAATAACATTTTTCCAGGTCTTTAGAC
ATAATGGAATACCTTGCAGTAATTAGATACACTATTGTAGAAAAGTATTG
ATGAAATGGAACGATGTTTGGATATCATATTGAGTAGAAAAGGCAAGAT
ACATTAAGTAGGAAATGTATCTTACAAAATAATTTGTGAGACACACTCCT
ATATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAG
ACCACAGTCTTCGGTGAAGTTTAAGAGATGATGCTGCAGCATGCTCAGAA
AGGCTTGGTATAGTTTTTTCCAGTAATTAAGGACTGATCTTAGGTAAAT
GTCCATCCTCTCTAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGAT
GGTATTTACCCCCAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAATA
AATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT
GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCCA
GAAGCTATTACCTTAATTGGTTATGTGGATTTCCCCTCATACTGAGCAGC
TGTGTGTGGTGTGTGTA AACATAGCCATACACAGTAAGTACAAGGGCAA
ATGTGATGGA AAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGTA
GAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCATG
TCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAGT
GTACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGGG
ACTCCACTTGCATGAACCTCTGGAATTGGGGCAAAGAACCATCATGAGAAC
AAGGGCTTCTTGAACCTCCCAGGCTCATTGGCTGATCTAAACCCTGTGT
CCCCCTTTCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGACT
GGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAATA
GGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCCACAGGAATTTGTT
TATACCTTTGGCATGGAAAAATAGCAGGAAATGAGTGATCACTGATAACTG
AGGATGCTATTATATTGGCCAAAGGAATACTTGTTGTTGTTGTCATA
ACCCTCACAAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTCA
AGTAAAGGATCTTGAGAACTGAAGGCAAACAGAGCTCCAGGAGTCCAAGA
CAGAGCCACAGACCACGAGGATCCCTGGCCAGGTAGGTGGTCTCTCTGC
ACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTGG
CCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTCT
AAATATGATCTCTGAGACCTGCCAGAACACCTTGCTCTCAGCCCCAGTA
GCAGCCTGCTCTCTCCAGGAGGCTTCCACTAACAGTAGGGCATTGCT
GGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAATGC
TAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA
TTGGTCCTTGGGAACAGATTTTGAGTGCAAAGAGATGGACTTCAGATGGC
CAGATGCACTGCTTCTTAGGGAATCTGTGAAAGCTCCCTGCATTTATC
TTAATACAGGCAGCAGATTTATGAGTACCCCCGAGGGATGGCCCCAGGT
CCTCCAGCCTGTGAGCATCCTTCTGTCTTCCAGCAGCACCACAGTATCTT
TATATGCTTTGGATACCTACGTTTCTGCCAGACATCTTGTCTGATG
TTCTGGCTGCCAAATTCTCTGTCAAGCGCTCCAATTTTTGTGTCTCTT
GATTTACCCCCAATGACAAAGGCAGTTGTGCTTCATGTATTTCAGGGATA
CTGCCAAACCACAAACAGGTTAAAATCAAATAGCAGATATCCCTGTTCT
AAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCGTCTTATTGTT
GAGTCTGAAGCCCTTCTGTCAATTTTATTTTTTGTCATGAACAATTTA
GTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTACA
CAAACCTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAATC
ACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTTGCTC
CACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAAC
TGAGATAGGGTGTGCAGAAATTTATATATATAAATATATCTCCTCCAACCC
CTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCTAAGATATTAGGG
ATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGTT
GCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACTC
AGCAAACCTTCTATAGAAGGTGTGAGTGGTAAGTATTTTAGGCTTTGCTT
GCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCAG
CCAGAGACGATCTGTAAACAAGAGCATGTAGTGTGGCATAAATATAGTA
CCGCG

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GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTTACATTTCAGAACAC
TTAATCTGCAAGAGTCCTTTCCAAGACCCTATACCTAATTTGTGTTTAC
AATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATAAACTATATCCA
GCCTTCATGATAAGTACATAAGAACTATGCAAATAAGGGGGAAAAA

CAAAGAAAAATACCTAC TACTAATGGTTCACCTTCTGAATAGCACAT....
TCATAATGATACAAGCACTCATTACTAGTCTAGGAAAATGAAGATATAAT
TGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGGTATAGAC
TAGGGCAGGACAAAGAACCTAAATCCTCATTCTTCTAAAGATAATTGTAA
TACGTAAAACTCAAAATTCAAGAAGTAACAGTAAAAGCGGTCAATAAGAA
ACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGGAAGAGGGCAAG
AATCTGATTATTTTTTGCACAAATTTTGTAAAACCATTTGACTGTTTAC
ATGTAGAACTTGGATCTTTTTTAAAAAACACAAAATAATAACTATTAT
TTTTTAACCTGGATTTTTTAAAAAGAAGATAAAAGTCTCATTCTTAGTAATT
AAAACCTCATTCAGGTTAGTCCACTCAAACTTATATTCGAAAATTAAAA
CTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGGAGTTTCGAGACC
AGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAAATACAAAATTAG
CTGGGCGTTGTGTAGCTGCCTGTAATCCAGCTACTCGGGAGGCTGAGGCAG
GAGAAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA
CCATTGCACTCCAGCCTGGGCAACAAGAGTGAAACTCCATCTCAAAAAAA
AAAAAATAAATTAACCTCTGGAAGTTGAGTTTGCAGATATTCAT
TATGCTCATTTTTAACTTGTATGTTTGGAAAATGTATGATGAGAATTGA
GGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCACAGCCCATTCAA
TTTTAGCCCGACCCACAGCTCCGGGGAAGGGCAGCAGGTCCATCCTTCA
CTCTTTCTTCACCTCTTTCCCTCTCTGCTCTTCCACCTCTAAGTTG
GAGCCCAAGAAGAGGCACTGGGAAATGGAAGTCTTTGTACGTGGTAC
TTGCCGGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGGAGGGAATG
CCCAGCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGTCCAGACATGTC
AGGTGGTCTGACAGGGCAAGCAGCAGGAAGTCATGTATGAGTATGAAGT
ATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGGGCGTGAGAAA
ACAGCACAGTACGTTCTTTAGCAGCTGTCTCTGCTCAGCCATGGGAGTC
ACCAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGAGATGTGAGTGT
AAAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGCCCTCTTCCCT
ACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACATGGTTCTCTCA
GAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCTGGTCAGCAG
CAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTCACAGGCAATGAGCTCT
CAGCAATAACAGGAACAGTGCTGGGGGACTGTAGCTGCAAGACCGATT
TCATGTAAGATGGCCTCTGAGGACTCCGAGATACACAGGCTGAGACTAG
CTGGCAGCTCCAAGTTCTTGGTCAGAAGAGAACAGGAAGTAGGGAAATTG
GAATTACTGTTACTACAATTCCTTTACATCCGCACAACCATGAGGTCCAG
AGAGTCTCTCTTATTTTTTTTTTAAAGACAGGGTCTCACTCTGTGCCCCA
GCCTAGAGTGCACTGGTGTGATCATGGTTCAGTACAGTCTTCACCTCCCA
GGCTCAAGTGACCCCTCTGCTCAGCCTCTCAAGTGGCTGGGACAGCAGT
TGCATGCTTACCAGGCCTGGCTTTTTTTTTTTTTTTTTTTTTTTTTTTT
TCGGTAGAGACTGGGTCTCTGTATTGCCAGGCTAGTCTCGAACTCCT
GGGCTCAAGTGATCCTCTGGCCTCAGCCTCCCAAAGTGTTGGAATTACAG
GCATGAGACACTGCACCCAGCCAGTATAGTCTTTTAACAGCTTTATTGAG
GTACGGCTAACATTGAAAAAACTACACAAATGTAAAGTATGCAATTTGAT
AATTTTGACAAATGTACACACCAGTGAAACTATCACTACAGTCAAAATAA
TGAACATATCCATCACTCCCAATTTCTCAGCCCCCTTGGTAACCCCTCT
CTCCCAACTGCCCTGCCCTAACATCAGACACTACTGATGCATTCTGTC
TCCATAGGCTCATTTACATTTTCTAGAATTTTACATAAATAAAATGACAG
AGTATATACTCCTTCATGTATGGCTTCTTTCAGCCCAATTATGTCAAGAT
TCATGCTTATGGCTGTGCGTATCCTTAGCCATCTCTTTGTCTTGCTGAG
TAGGATACCAATTGCATAGACAGACCAGCTTGCTCATCCATTCACTCTT
GACAACGTTGAATTGTCTCTGTTTTTGAATGACAAATAAGGTTGCTAT
GTACATTCTGTATAGACATTTGTAAAAGCACAGCATTTTCACTCTCTTG
GGTAAAGACCTAAAAGTGGAAGGCTGAGTCATATGGTAAATATATATGT
CTAACTTTTTAAGAAACTGTCAAAGTGTACCCAAAGGGATTGTACAATT
TTACATCCCCACCAGCAGTGATGAAAATCCCGTACTTCCACATCCTCA
CCAATATATGGTGTGGTCAATCTTTTTAATTTTGGACATGNTAATGAGTG
CAAAAACAGGCTGTCAAGCATAGAAAAAACACTTGTCTTGAATGGTCAG
TCATTTACAAGTGGAATTCATTACAAACCGGTAGTTCTACTGGGTAAAC
TATGCTTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

CAGAGACAAGGCAGAGC...TGATAAGAAGGTGACCTGGGCTCTAGCTCT...
GCCTATCACCTAGTAAAATATTAGTTAAGTAGCCATGAGTAACTCACTTA
ACTTACCACAGGCTCCATTTTCTTATCTGTAAAATAGGAACATTGAAACA
GCTAATCCCCAAGGTTTGTGGATAATCAGAATTACAAAGATCAATGACAT
TTCTATGAGAGAAACATATTTCCAAGTATTTGATGGAGTACATCAGACAC
AAAGGAAAGGAAACTGAATATTTTGGAGTTTTTTTTTTTTTACCAAGAAA
TTCACATTTTGTAAATTTTTCAGAACTACCTCCTGAGGAAAGTGTAGCTG
CACCCATTTAGAAATGATAGAAAACATCAATCTGTCTGATTCCAAAGCCAA
GTTCTTGCTACAACGAGAAATGAAACAACCTGGATCCCTACAGATGCAGAG
ACCTGGGCCCCACAAATGTGAATTTCTGTTCCCTACCGAATAGAGTTACA
GTTCCATAATACAGTACTCCCTCACTTTTCCACAGTCTCACATTCCACAG
TTTCAGTTACCCACAGTCAACTGCAATCCAAAAATATTAATGAAAAATTC
CAAAAAATAACAATTCAGAAGTTTTAAATTTGTGCTCCATTCTGAGTAGCG
TGATAAAATCTTGTGCCACCATCCCACCTGTCCAGCTTATCGTTAGTCAT
TGACATCGTCTGCTCCTGACATCCAACCATGACATCATCATGACTCTAT
GATCCAGGATCACCGAAGCAGATGACCCTCCTTCTGACATATCATCAGGC
CAATATCAGCCTAAACACTGCATCACTATGCCACATCAGTCACTCACT
TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCACAAGAAGAAG
AGTGGGTATAGAACAATAAGATAATTTTGGGGCAGGCATGGTGGCTCAGC
CTTGTAAATCCCAATACTTTGGGAGGCCAAGGCAGGAGGATCCCTTGGGCC
CAGGCATTCAAAACCAGCCTGGGAAACATAGTGAGACCTCCTCTCTCTGC
AAAAAAAATAAACAAATTTATCCAGATACAGTGGTGCATGCCTGTGGTC
CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTTGGTCCCAGGAGGTC
GAGGCAGCAGTAAGCTGTGATCGTGCCACTGCACTCCAGCCTGGGCAATA
AAGTGAGACCTGTCTCAAAAAAAGGTAATTTTGAAGAGAGACCAC
ATTATACAACTTTTATTATAGTATATTGTAGAATTGTTCTATTTCATT
ACTTATTGTTGTTAATTTCTTTCTTGCCTAATTTTTTTTTTTTTTTG
AGTCGGAGTTTCACTCTTGTGCCCAGGCTGTAGTGCAATGAGACGATCT
CAGCTCACCGCAAATCCCGCCTCCCGGTTCAAGTGATTCTCCTGCCTCA
GCCTCCCGAGTAGCTGGGATTACAGGCGCCTGCCACCATGCCAGCTAAT
TTTGTATTTTATAGTAGAGCGGGGTTTCTCCATGTTGGTCAGGCTGGTCT
CGAACTCCTGACCTCAGGTGAGGCCTCAGCCTCCTAAAGTGCTGGGATTA
CAGGCTTGAGCCACTGCGCCTGGCCTCTTGCCTAATTTATAAATTAAAC
ATTGTACAGGCATGTATTAATTTATAGGAAAATCATAGACATATAGAGT
TGGGTACTATCCACAGTTTCAAGGCATTCACTGAGGGGCTTGGACACGCC
CTCCTCAGATGAGGGGGGACTACTGTCTCTCTCAATCATTTCTTGATTC
AATCCTCAACACAAATGGTTTGCCAGGTCTTGCTCTGGAGACAAAT
GCTAAGGATTTAGAGGGGAAAAAATGTAGTTCACTGGGAAAGTCACCTCT
GCTCCACTGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC
ACCCCTCACTCTCCTTCAACCTGGAGTATTCAGGAGTCAATCATATTTCA
GGACCACCAGGAGCAAACTGGGAAAAAAGTGAAGTGCCTTGAGGAAAGCAA
TCAGCTCCACAAGGGGCTTAAGAAACAAGCTCTGGGAGGAGTGGTTGGAG
AAGAGTTGGGGACACATCAGAAATGCCATCAAATTTCTAAGGGCTACCTC
GTGGTGTGACACCTGTGTCATCTTCAAGGACATAAACAGATGGGATAAGCA
GATGAGATTACAGAGGACATCAAAATATTGGCTCCCCAGAAGGGAGAAC
ATTCTAGTAACAGAGCTGCCAGCTGCAGAGTGGACTGTTTCAAAAGCA
ACAGGTGCCCTGCCTCTTGAATCACCATCTTCAAGGAATGCAGTAGAAG
GGACTTAACTCCTGCCCTGAAGAAAAGGTTAGGCTAGGGAAACAGCTCCA
AAATTTTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTTTCTAAAG
CCTTTGTTTTAATGAACTAAAGAGCTGGGACAGGAAATGCCAAATTAAT
TAATAGAGCCTTGCTTTAAGACAATGCAAGTGGATGGTAATGAAGGAATG
AGTCTTAGGCCTTGGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA
ATTCTGTTCACTAGATTTGCTCAGAAAGGGCCAGACGAGAAGGATTTTTC
TAAAGGCACCTACTACAAAAAGCTGCCAAGGCGTCCAATGGAGCCCAGA
GAGAATATGCTAACAAATAAAAGTTGAACACCCTCAATAAAAAAGGGTAA
AAGTAATTAATAGAAAATTACTGAAAGCTTTTTTGAACCAAAAGTAGTC
AGCATTGGTAAAAGTCTACAAAAGTGGACACTTTCATATAATGTTGGCAG
GAGGGTAAAAAGACATAACCTTTTGGAGGACAATTTGGCAACAGAGTAC
CAAAAACCTTACAATTGAAGAGAACTTTGGCCTGAGTGCAGTGGCTCACA
CCTGTAATGCCAACACTTTGGAAGGCCAAGGTGGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

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CAAAAGTTTSGAGACCAGCTGGGGTAACACAGTAAGACCTCGTCTCTATG
AAAAATAAGAAAAGTTAGCTGGGCA TGGTGGCATGTGCCTGTGGTCCCAA
CTACTTGAGAGACTGAGGCAGGAGGATCGCTTGAGCCTCGGAGGTCAAGG
CTGCTGTGAGCCATGTTCTGCGACTGTTCTCCAGTCTGGGTGACAGAAT
GAGACCCTGTCTCACCAGAAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA
GGAGAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGATGGAAGGAAGGAAA
GAGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAA
AAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGAAAAGAAAGGA
AGGAAGGAAAAGAAAAGAAAAGCAAGCAAGCAGGAAAAGGAAGGAAGGAAGGAA
GGAAGGAAGGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA
GAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGGGAAAAGGGAAA
AGAAAAGGACAAAGAAAAGACCTTTGAACCTGAAATTTCACTTTTAGAGA
TTCATCTTAAGGAAATTCATTCCAATAGAAATTTATCCCCAGGATTATCT
AAATATTTGCTTTTATTTTCTTCTAGTAATTTTATGGTTTAACTTTCTCA
TGTTTAAACCTTTAATTTATTTGGAAATTTATTTTGGTATGAGAAAGTGTG
ACCTTTTGTGTTTACTTTAAAAAAATGTATTACGATTATTTTATTTAG
AGACAGGGTCTTGCTCTGTCAACCAGGCTAGAGTGCAGTGGTGTGATCAT
AGCTCACTGCAGCCTTGAACCTCTGGCCTCAAGCAATTTCTCCCTCTTCAA
CTTAGGAGTAGCTGGGACCACAGGCATGTACCACCATGCCCCAATAATTT
TTTTTATTTTTGTAGAGACAGAGTCTTGCTTGTGCCCAGTCTTGCAAT
GTTGTCTCAAACCTCTGGGCTCAAGTGATCCTGTGCCCCAGCCTTCCAA
AGCACTGGGATTACACGTGTGAGCCACTGCGCCAGCTGCCTTTTTATTT
TTTAATTTTTCAGATGCTTTGTTGGTTCCAAAATAGCACTTATTAACCCA
CGCTTTCCCCCTCTGGTTTTAAATACTGCAAGTTTGGCTTTGAAATACAA
CCCCTCTCCTTATTCAAGGCTACATTCAAGGAAATCTGAGACCAAGAGTCT
GAAGGCCAGTTTCTTCTCAAACCCAGGAGGTGGTAAATGTGTCACTT
CCACACTTTCTATCTATTTCTAAGAACTCCTTCTTTCCAAACTCTGACAT
GCCCCCTGGCTCAGGTCTATAGAAATTTCCAGGGTCCACAGACAAAGCAGA
ACTCACTTATGGGGAATCTGGGAAATACTTATCTGTAAACCTGCCCCA
TATGGTGA CTGAGATTGTCTAAAGCCCAAAGCATCATTTTCCACCCCAA
CCATTTCTCCTCCAGACTTCTCTATTTCTGTGGTCCAGAGTCAAGATCT
TGATATTACCCTAGAGTCCCCCTTCTGCTCTCCTGCATACCAGATGCCC
CTCCCTCCCAGATCCATTCTCCACCCTCCCTCCCATCAGTTTGGTGGG
CCCATCACCGCTTCCCCTGGCCCAGGCTCTCCTTTTGTGCGCTTGGAGCA
GCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTGTTGTGT
TCATCACTGTGAGAACTCTTCTGCATCCCCTCACTACTCTGCTGAAAACAC
TCTAGTGGTTCTCTCATTTGCTCATTAAATGAAAGTCTAGATATTAAACGTAG
AAGGCCCAGCACAATTTGCCCCATGCCACCTACCTCTCTAATCTTTTTCT
CCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTTATTGCT
CTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTAAACATTGCT
TTCAAGTATGGAATAAGAAATTTTATTTATTTATTTATTTATTTTGA
GACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCAGTCATA
TCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGCCTCAGC
CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG
AATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAAATTACAT
TGTACCTAATGCCCAGCATTTACTTTTTTCACTGGGTCAATAGCCCTCA
CTTTGGCAAAGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTCCAAACTC
ATCTTTTGAAAGACATAAGTGCTGTAAAGTTGTACCACATTAGGTTCTAG
GAATTTTTCATCAAAGACTTTATCAGACTATTTTCTCTAAGTTGAGAAA
GAGCTGGGGGCAGAAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA
TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA
GGAGCCSGTGATGATTTTGGCTTACAGGGAGGTGTGTACCACACCGATT
TTATCTCTACGTGGATGAACCACAGCTGTGCGCTCCCTTGTCTCCAGGAC
ATCACACTCTCCACATTTCCCTCCCATCTTCCGGCTTCTGCTTCCCGGGC
CCTCATCTGCCCCATCCTGGGTGAACACTGGTGGTCAACTGCTGGGCGT
ACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCACGGC
TCGCACTGCAGAGGAGCCGATCTCTAGCTCCAGCCCATCTGCCTCTTCT
GAGCTCTAATTCATGTAGGCGACTCCTGCCGGTGTGCTTCCAGGGCC
ATCATACTTCAAAGCAATTTCCCTCAGAACACCATGTCTGGCTGCTCC
CTCCAGAAGATACATCTCTCAAGCACATCCCCGGGCTCTCACCTGGATG

FIG. 3 (51 of 52)

ACTGCATTACCTTCTC ACATTTGCCCTCCTTTGGATGTATATAGA.
STTTTAAATACAAATCTGATGTGCTTGCTCTCCTGCTTGAAACACCTCA
AAACTGCCCTCAGGATAAACCACTGCCCTTGACATGTTTACAGGTTGCC
ATGGCCTGGCCCTGCCATCTCTTCAGCCTCATCTCATGCCCTTGCCCC
TCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTCTCTAACAC
ACCATAGTCCTTCTAGTGTGGGGCCTCTGCAAGTGCTGTTCCCATTTGCC
TGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCATCTGATTAA
TOCTACCCCTTCCTAGTCATGATGTTGCTTTCTCAGGGACTCTCTCTGAC
TTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAGCACTCTGT
ATTACTCCTTTCTTAATGACCACCTGCTGTAGACTGAATGTTTGTCTTCC
TCCAAAATTCATATGTTAAACCTAGCCCCAAATGTGATAATATTTGGAG
GAAGGCTCTTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT
AAAAGAGACCCCTGAGGGCTCCCTTGTCCCTCCACCGTGTAAGGATGCA
ACAAGAAAGTATGGTCTATGATCCAAAAGCAGACCTTGCCAGGTACCC
AATATGCTGGCACTTGAACCTCCAGCCTCCAGAAGTGTGAGAAATAAAT
TTCTATTTTTTCATAAGCCACCGAGTCTATGGTATTTTGTATAGGAGCAC
AAACAGACTGATGTGCCACCCAACCATGATTATACGTGTAATTTATGGTT
TCTCTGCTAGTAGGGATGCACCATGGGGTTAGGAACACGCTTTTCTTAT
TTCCACACAGTCTTAGCTCTAAGCATGTTCTGAATCAAAGATCCCCA
TCTTTTATGAATGAAGGAGTCAGTGAATGAATTAATGAAAGAACTGATAA
CCCTCAATAATTATTCAGCCTTTTATACCTACTATTAACAAGCTTGCAAT
TCTACTCCAAATTTATTTGGGCTTTAACTCTATTTTGGCCAGCCACATTT
GACATTCCTGAAGTAAATCTATGCTTTCCATCCTAAGTCAAGGAAGGAC
CTGGACTAGTAGGGCCAAGAAAGGTCTAAATTCATGGGTGGGAGAGAGA
GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG
AAGGCTGGACATTTGGAGAGAAGGAAAGGAAACTGACACTAAACCAAAC
AGTCTCACAAACACAATCTCATCTTCCAAAACCTCTGTGAAGTAAGAAAT
ACTATCCCAAGGGCCAGGCAGTGGCCCATGCCTGTAATCCCAGCACTTT
GGGAGGCCAAGGTGGGTGGATCACCTGAAGTCAGGAGTTCAAGACCAACC
TGATCAACATGGTGAAACCCCATCTCTACTAAAAAATACAAATTAGCTGG
GCATGGTGGTGACACCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGG
AGAATCATTTGAACCTGGGAGGTGGAGGTTGCAGTGAGCAGAGATCGTGC
CACTGCACTCCAGCCTGGGTGACAGGGAGACTCCGCTCTCAAAAAAAAAA
AACAAAAAAAAAACCAAAAAAAAAACAAAAACAAGAAATTAATATCCCAG
TTTTGCAGATGAGGCAATGGAAGCTCTAAAAAGTTAAGTAGGAGAAACAA
ACATGAAATGTATGTCTTATGCTTTTCTCATCTATTTCTCAGCCTGG
AATGTCCATTCTCCCTCCACTATGCAATCTAACTCTTCAAGCTAACACA
TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTTAGCCTCACTTG
CTCCCTCCCATCCCTCTGTTTCTTTCTGTTATAACACTTCTCTATTCT
GCTGGCATCACAGTCATCTCCACCTGCCTTCTCACAAGTTAAAAAGCTTG
TTAAGGGCAAGTGGTGTCTTTGCCACCTCATTCCCCAGGGCTTCTAACA
CAGTGCCTCATGCATGACAGAGTTGTAAAAACAGGTTACCAAGCTGGCTTC
AGGCAGGTTTGCATGGAACCTGTGCTTTACAGGAATACCTGCTCCCCCAG
GCCCTGGGTCTTCTCTGAGTCCAGGCTCAGACTCTCTCATCTGCTCG
TTCTCTCTTGGGGAGCCACAGTAACTTTGAGCAACTTTGCATGGGATAGA
ATGGCCTATTAGGGGCAGCAAAAGACCCCATGGAGGGAAGAGTACAGAA
AGGAAAAACGATAATCATATTTTTTAAGATGTGCATTTTCTTAACAAAA
TGCTCTAGTACTTGTCCAGACTTTCAAACCTCAAAAACCTAAGCGTCTTT
TCTTGAAGATCATCAAAGGCCCCAGTGGTCTTTCAGGTATGTCAAGCTTT
CTAGAAAAATAAGGTAAGTCATAATCACTTAACACACATGGCTAAATGGC
CATTTCTTCTAATTTATCAGCACTGTTACATATTTCTATACTAGAAAA
AATTTATATTTATACTCAGGGTGGTAAGTTAAATTTGCCATCGAAGTAAA
GCAGAAAGAGCGTAGCATGTATGTATGTAACTCAACTGTGCATGAGAC
AAAGATGTCTTGAGGAGAATGAGTCTAAGATGCGCTGAGCAATAGTACC
C

FIG. 3 (52 of 52)

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>Contig1

GCACCCATGTTTCTAAAGGGCATACAGCCATAATAACAGGATGGGTGAG
GATATAGACAGCAGATGACAGAGAGGAGAGTGAAAGCTGGGAATCCCAGC
TAAAGGCATCAGGTTTATGGAATGAGTAGGGGACAATACTGTGTGTGTTT
ATACACACATGTATATGTGTGTATATGTATACATGTTTATGTATATATAT
AATTATATGGTACCATTCTAATTGACAAAATAATCTATCACATTTTACA
TTATCAGATTTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG
TGTGTGGGCTCTTACCCATCCCATGCACACCTCAGCTCAACCACTGATG
GATGGATCATCTGCCTATCAGAGGTGGCATATTGAGGTGAATCCATGGCC
ACAGCTGCAGCACTTCTACCCACGCAGAAAGGCTCCACAAGAGGAGGCA
CACCCGCTCTGACTGTCCCTAAGCTCCTGACATCTTACCCCATGAACT
GCTGCTCCTGGGTGCTTCTGCTTGGCCTGCCACCCCTTGTAAGTGTCT
CACCATTGACACAGCTGGTGCCCGATGCAC

>Contig2

NAAAACGAATCGTCACTATTGAAGCCTGTCTCTCANC GGATCGTGACTAA
GAACCCCTCCTTGCTTCAAGTTGTCTGCTTTCTAGGCAGAGCCACCC
TACATCTTAAATATATTGATTGATGACTTACGTCTCCCTAAATATATAA
AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG
ATGCTCTGTCTCATGAGTGGGTGGGTGTTCTCAACCTTGGAAAAATAAAT
TTCTAAATTAACGTGAGACCTGGGTGAGATTTTGGGGTTTACAGCAACAA
TTTAAAAAACTCACCATTGACCTGAAATTTTACCTTATGCTGTTGCTCA
CACTCCTCCATGAAAATAGACGCCATCCTATGAGTTCCCTCAGCCATGTC
ATGCCACACTTCCAACATGTGTCCCATCCACCATCTGTCTTCTTATTGC
TGCATCCTACCCAGGCCCTGATCTCTGGACCCATTGTTGTATAATTAAGA
ATTTGGGGCTGGGCATCGTGGCTGTGGCTCACTCCTGTGATCTCAACATT
TTGGGAAGGTGTATTAGTCAGGATTCTCCGAAGGATGCAACCCCTAGGGA
TCCTCTCTATGACCCTATGTCTA

>Contig3

CGCGCTCAACCGACCGATTTGCGCGAACCTGCCCATGCCCGAGGACAGTG
TAATCCTAAAACGTCCCCTGAATCATAAGGATATGAGTGCGAAAGTACGG
TTCCCTCTGTACCACTTTCTAACAACGCTATGTCCGATCCGTGCACTAA
CCCCGCCCAAGTCACTGAAACACTGATGGGCGCTTCTCTACAGGTATCC
AGGGCCAATACCACTACTCCCTCCTCCTGTCCCTTCCACTCTCTAG
AGGCCGCGGATGCCATCCTCTATTAGCACAACCGAAAACGACGGTGAAAG
TACCACGAAGCTCACGATCTGATCGGTGCGCCAATGCGGTTACAACGGCT
GTCATCCCAACCCCGTCCCATCCTCCATATTGCCCCCCTATGAGGAT
GGCCCTATCATCATGACCTCCAAAATTCTGTCTCTCCCGACGTAATGCC
GCCCTCGAACCGCTGACACCATCAAGTCNGTCACTCCCAAATACTCC
TCCTAATCACCGGCCGAGTATCCCCGGTTCCACAATACCTCCTTGAGAC
GGGCCGATATCACACAC

>Contig4

NGGAGTTTAGGTCAACTAGTAACAAGTGGGATTTGCGACTCAGGTCTATC
TAATCCTCAAACCCACGTCTTGACCCCTACACAGACTGCCCTCCCTCAG
TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTTAAAAATCCA
TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCAATGTTCTGAGGCT
CAGAAGGGCCAGGCAGGAGGGAGCCGCTCTACACAGTCTGAGCAGAGT
GGGCTGTGTCCCGGCACAGCAGGGGAGATCATAAACAGAATTCTGCCCTG
GGCCCTATTTAAGTAGGACCTTTAGGCTGCCGTTGTCATGACCACAGGTC
CCANGTCTGCACGATTGGCTGTGTGTGGAAAATCTTCACTCCTTGCGGCC
TTGTCTTTGGCAGAGACCGCTGCTTCTGATGGCCACCAGGGGGA
GGCGCTCCCTCGGAACGGTTTGAANGGGAGCCTCACCCACACGTGCCT
TCCGTGGTACCCAGCACAGCTGCTACCCATGGTTACCCACAGGCCCAGC
TCTGCTCTGAAGAAGGAGGAGTGGTGGCGATCANGCCTTGTCTGCATCCC
GTGGCTGCCCTTTCTTTTCTTT

>Contig5

GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACCACGCCTGGCT
AATTTTGTATTTTATAGTAGAGACGGGGTTTCTCCGTGTTGGTAAGGCTGG
TCTCGAACTCCCAACCTCAGTTGATCTGCCCGCTCAGCCTCCCAAAGTG
CTGGGATAACAGGTGTGAGCTACCATGCCTGGGCTTATATGTTTCTAGTC
CAAACATTTAGCTACCTTTTTTTTTTTTTTGGAGACGAAGTCTCACTCTGT

FIG. 4 (1 of 61)

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TGCCAAGCTGGAGCACAGTGGCACAATCGTGGCTCGCTGCAGCCTCAAC
CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA
CTACAGGTACGCACCACTACACCTGCTAATTTTTTTGTTTTGTATTTT
TTGTACAGATGGGGTTCTTCATGTTACCCANGCTGGTCTTGAACCTCTG
GGCTCAAGCAATCTGCCTACTTCAGCCTCCCAAAGTGCTAGGATTACAAG
CATAAGCCACCATAACCGGCCTACCTACTTTAACTTGTGGAATTTTCTA
TAAGGTCANGGATGCCTGNGGGAACAAAAGTTTCTCCCTTGGTATATGCA
AGTAAAATCCACATGCTGCCTCCC

>Contig6

AGGACTGTAGCTGTTGTCTAGTCACCAGGCTGGACTGCTTGGCATGATCT
CAGCTCACTACAACCTCCACCTCCTGGGTTCAAGGGATTCTCCTGCTTCA
GCCTTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCGGCTAAT
TTTGTATTCTTAGTAGAGACGGGGTTTCGCCATGTTGGCCAGGCTGCTCT
CAAACCTCCTGCCCTCAAGTGATCTGCCTGCCTCGGCCTCCCAAAGTGCTG
GGATTACAGGCGTGAGCCCCCGGCCACATGTAAAAGTTTATATCTCTGT
TGTTTACCTTGTTTTTGACCTAGTCTTTCAGTGATTTGAATCTTGATTCT
AGTCTTTTGTATTTTAGTGGTACTTCCAGCTTGTGTCTATCTGTGGAT
GACATATGAGTCTTGCTTCTTCATGCCAATTTAAGAAGACTGAACGGGAA
TAGGTCAAAGGCATGGCCATGAGCGATTTCTCTCCAGCTTTTCATGGTGT
TCAGCTTCAAATCTATTTCACATATTGGACCTGCAAGCCATCATCTTATCC
ACAGGCTATCATCATAGGTGAATGTAAATTGGGTTTAGGTGGCCAAGCTG
AACGTGAGATATNTTC

>Contig7

AGCATGTTCTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC
AGTTACCCAGCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAG
CATGACCTATTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGA
GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACT
ATTGGGGGTTTTAAGCAGGGATATAATATTCAATTCAGCATGCAGTAAAA
GGTCACTGGCACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGT
CTGTTTTGGAAATATCACCTTGGCTGTGAGATGAAGAACAGGTAGGAGGG
TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTTGTG
TGGACTGTGGCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAA
GGCATGTGGGAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG
GTTAGAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCAGGTAT
CTGGGTGGATGGTAAGACATTATGGACTAGAATCGAAGAGGAGGTGGGG
ATGGACATTCTTCCGTTTAGAGGGGTTCAACAGGAGGATTTGCCGGAAC
ATGGAGAGGATTAACCAGGAATCCGGTGCCTTTTTCCAAACTGGGTTGGA
GGGG

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GGTGAATGCTTTGGCACGCTGTGTAGATTTTAGGTGACGGGTGGTGACAA
TGAGTCCGTGTCGAGCGCTGATTTTTTCGGCCTTTAGAGCGAGATTTATA
CAATAGAAATTTGGCATGAGATTGGATTGCTTTTAGTCAGCCTCTTATAGC
CTAAAGTCTTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT
TTCCAGTTTTCCGCTCCTAGGTCTGCATATTGTACTTTTCTCTTACTCG
ACTTAACCAGTACCAACCCAGCTTCTCAACGGATTTATACCATGGCACTT
TAAAGCCAGCATCACTGACAATGAGCGGTGTGGTGTACTCGGTAGAATG
CTCGCAAGGTCCGCTAAAATTGGTTCATGAGCTTTCTTTGAACATTGCTCT
GAAAACGGGAACGCTTTCTATAAAGAGTAACAGAACGACCGTGTAGTGC
GAATGAAGCTCGCCATACCATAAGTCGTTTTTGTCTCCGAATATCAGACC
AGTCAACAAGTGTCATGGGCTCGTATTGCCCGAACAGATTAAGCTAGCA
TGCCAACGGGATAAACGAGTCGCTCTTGGTGGAGGG

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GGGGTGGGGCGCCTGGTGTCTTAAAGAGGATCTCCTGCCAGAAATGGTG
TGCTGACACTGTTGTCTCTCCTGGTGTGGAACCTTGGTGGGAAGAAAGGT
TGGAAAGGGAAATTTTGATCCTTGGATTTAACCCGAGTTTGTTACTGATG
CTCACAAGACTAGGGGAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC
TCANTGAGCTCCACAGAGCTGGAACACAGGCACCAGGAGGGATTGAGAG
CAGGCCTCAGTGACGTCAGCTGAGTGAACCAATGAGCAGGTGATGGGTC
CAGGCAGAGCCCTGTCTCTTTAGGCAAAAACCTTGAAACACCGTTCCC
ATCCTAGCCTGTGTTCCACCCAAAGCTGGCCAGTCTCCAGGCCCTGCCTG

FIG. 4 (2 of 61)

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AGCCCCAAGGAAGTGGTATGGTGAAACAGAAGGGCCATTCTGTCCAATG
TGTGAGGAACCTTCATTTAGACTTGTGGGAAGCCCTGATGTTCAAAAACC
TCAATGATATCATTCATTTTCCCCATCCATTCAATGCCCATCCAATGCCC
ATCCGTTCAATGCCCTTCCATTCTCTTCAGGGAAATGAAAATTGTTCA
GAAATCCTTTCTCTTTGAGAAACCAACCAAAACCAAAACCGGAAATTCA
CTAAACTAGCCAAGACACAATCCTGGGTTATTTTCTTTTCCCAAACCTC
CTGTGTTTAAATTAATTCTACCCTGGTTCTCGGCCCTTACTGCGAAGGTG
AACTCACCTAACCTCTCCCAAACAGAGAAGAACTTCTCTTGATAAAATG
GGTTTTAACTTCTAAAAACCCCC
>Contig10
GCTATGGTTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT
CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT
CGTTGATCCATCTCTGTACGCACTTGTCAACATGGCAGGAGTACGGGAGC
TGCGAGAATCCTCTCTGTGATGTCCACGGAGCATGCCGTGAGACAACG
CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC
ACACGTAGGAGTCTTAGCTCACCAGCCGTATCTAGGTATACTGTACTCGC
GGATACTCACTCGTGCATGCGGCAATAGATCGATACGCAGTCGTACGCC
CATGCTCTCAGTGTGTGACCTTCTGGCGGTAGCGTNGTGGGCGCTATTAC
TGTGCGCAGCAGGCGCNTCGTACATGTGTGGGTAGCGATGCCAGGAGCT
GTAACATAGCAAGTCGCCCCCTACTCCTATCACTATCCCTACGCTGGAC
CGCACTCGAGATCTGAACGCACGTCTTAACCTGCCAGTACTCGTGAGACC
TATACTGCGCAAGCCTTGGCTAGGAGATCCTGCAGCGCCGGCAAAGAATC
AGCTATGATCCCTTGGCATTATCGCACACGCACCATAGAGTATGTGCAT
ATTAACCTCTGAATGTGCTGCAAGCAGACGGTTGCTCAACATATATATGG
ATGTGGGGAAATCGCCCTGGTCACCGCCACTTGGCGTCAGGAGGCACCG
CACGTCTGAGTGTACGCACGTTACTC
>Contig11
GGCCGAATGGTGAATTCATCCGTCTCGAGGGGGTGAAGACGGGGAG
TTATGCTGTAATGGCACCGCTCACCCTGGGCTTATGAGCAGACCTAACC
TCCCANAGTGCTGGGATTACAGGCATGAGCCACCGTGCCCGGCCAGTAT
CTGAACCTCTGTGGCCAGGCAGAAAAGGTCTGTGTTACTCGTCTCCTTT
ATCATTCATGTCCTATTTCTCCATTTGCTAACATTTATGTTTCTGCTCC
ACTGGATTCTTTGGATTTTTCTAGAACATACCCATGCTTTGCATTGCCTT
GGTCTTTGAATATTTGGTCCACTTTTCTGCAAAGTCCCCTCTCACCTTA
TCTTCTGGTAACTTCCAGCCAACACCTCTTTACTAACAGAGAAACAT
GGTTCAACTGTGCACAGGCTTGACAGAACTGTTCTCATATTGTCTTGT
CATTGTCAATGTGGCAGAGATGCACCTTAGATACCTCTTTGAGAAAGGAC
TCACTGCCAGCTGCCTGGCACGTGATGAGCTGATAGCTCCAGCTATAGA
CTCCTTTAGGGTCAACCTCTGCTTTCCAGTTGAGATCATATCCTTTGCAG
GGTGGCCTCCCCAGTGATGACTAAGGCAGTGTTACAATGGCCTAGTCATT
TCCTCCCAATGCTGGACTCCCAATGAACCATCTGCTCCGGAGCTTCCAC
TGGGCAGTCAGAGACCTTAGCTAGTCTGCCTCCGAATCAGAAGGCTCTCT
CTTGCCACTCTGGCC
>Contig12
GCTGTGTCTAAAGATTACGGCTGTAGTTCCAACTCCCGCCGCCCTCTAC
TGTGTCTCTTAATGGCAGTCATTACCATCTTCTGTCCCTCCCCTTCA
TTTCTTGGATGGTGACTGTCACTTTGCTGCAACAGAACCCTGTCCCAATC
CTTGATGGTTCAATACACACATAGACATCTTTTTAACAGGGCGGCCCTCT
CAGGTCTTTAATTTCTTCCCTCCAATAACCTTGTGATGATCCCCAGCT
TAGCCACTTACTGCCAGATCATTACCAGTAACTCCAGCCCCCTCCTTAATT
CTAGTTTCTAATATCCTAATCTGTGACCTCACATTCCAACCTTCTTCATT
TTATCCCCGTAGTCAAAAAATCCTTTGATCCATGCAATCCATTAAAGTCAT
CTACCTTTTACCATTCTTCGCCCCACTAGGGTTCTCATTCTTTATTAC
CCATATGAAATTCGAAGGCCTGTTGGAATCACTCCCTTGAGCCACTGTC
AATACTTCTGCCCTTTTACTTCATCACCTTATGTGGCAAAACACAGC
CCTGGTGGAGTCGATCCTTACCCCTGCTCTGTGCCAACAGCCGCACACGC
ATGGCTGATGGAGTTGGAAAAATCCACACATGCAGTGGGGCCCTGTATGT
CCATATACGTATCCAACTCCAGCCTTGCAATATGCCTCAGTGTGCTGCTGA
CAACACATTATATGTTTTCTTAGTTCTTCTCAGTCTCCTGGGTGCTAGG
TGAGTATCTCAGACATCCTTCTCTCTGCAAGCTCCAACACCTCCACG

FIG. 4 (3 of 61)

TCACATTCAACTGATGACIGTGTCTCCTATGTCACCTTAGATCACAGAGGC
ATACATAAACAAATCCCAGCCACTGCCAGCACTCTGCACATCTGCGAGCA
TGGCACCCCAATCTAGGCCTTTCTGCTGTCACTTGGGGTGAGCTGATT
ATACTCGATCCTAGTCATTTCTACTTATGCAC

>Contig13

CTTAAGGCCTCCCTCTAACATTTTAAATTTAAGATTGAAAAAGCAAAGATT
ATTCTGTTTTGGCTGCGCCTATAGTAAAGTAACCCCTATGNCAAATTTTG
ACACCTTATAGTATTTGACAGGGATAAGTATAAAATTGCTTGATTGATAC
ATCCACACCCAAATGTATGCTGGGAATGATTTTGTTCACGGCACTCATT
ACTTAATTTTTAAACTCTTATTTAAATTTGCAATGTTTTAAATGACCAT
CACTTAAAGTAGTAATCAACAGAGGTTAGGAGAACATAACAATACTCTTT
CTCTTAGAAAATACAACAGAAATATAATTTTTTACAGTTTTGCTCCCAAA
CTTTCTCTGTAAATAACATGCCTTACTCACCTTTACAATAGGTTTGTGT
GAGAATCTTGTAAATGTAAACCTGGGTGTTCTGTGAAGCATTTTTAAACT
TCTAGTTTACACTGACTCTTATTCAAGTGTTTTTAAAAATATATTTAAAA
AACTGGCCAGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGG
CCAAGGCCGGCAGATCACAAGGTGAGGAGTTTGAGACCAGCCTAGCCAAC
ATAGTAAACCTCGTCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGT
GGCGGGCGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGAAGAATCG
CTTGAACCCGGGAGGCAGAGGTTGTGGTGAACCAAGTTTGCGCCAATGCA
CTGCCAGCCTCTGCAGNGACAGCC

>Contig14

GGGGGCGGGCCGAGTGATCCTAAAGCCCGCTCGCTTCACAACAAAGCCTA
ACAGTCCCAATCACTTAATGCTGCATTTATTCTGGGGAAGCAAGTCTCCT
TTGCACTTTACACAGTGAGATAATCAGTTTCTCATGTGGACCACTGGGCC
AGGAGGGCCTGACAAAGGGCAGTCTACATTTTCACTGGAACTGCTCCC
AGAACTATTTCTTTCTAGTTCCACCTCGGTCTGAGGTGCCTGAGGAGAG
GGACTCAACAGAGGAAGCAGGAGCATAGCTCAAAGTCTCAGAACATGGAA
GAGGAAAAGAATCCTCACAAGATTACGTAACCTACAGGCGTGTGTGCTGCT
TCAGTAGAAGTTTCTCTCCCTCAATCCTGTACACTTTTCCATACATTAC
ATACTCAAACCTGGTCAGCCCTATGGAGCAATAGCAGCAAAGTTATTCTTA
ACAGTAATTAACAATATAAAAGATCCCATTTAAAAATGGTTACTGGTCAG
CCGGGCGTGGTNNNTCNANCTNTAACCCCANCACTTTGGAAAGCATGCG
GGCGATCCCAAGTCTGATATCGAAACATCTGCCTAACATGTGCAACCCCT
CTCTACAAAATACAAAAATATCCGGGCTTGTGTTGGCGCCGTTATCTCA
CTACCCGGAGCTAAGTAAGAAATGCTTTACCTGGAAGCGATTTTTTTACT
TATATCCCTCTCTTACCCGGGCGCGACCAAATCTTTAGTATAGGAAAG
TTTATTGTTTTATGCCTTTGTCAAGGCTCTACTGTATCTTTCTGTCCAC
TCAC

>Contig15

GGTTCTGAACAACAGCAGGCGATTCTAGCCCTGTACCCGGGGCATTGTC
CAACACTCGACAGGGCTGAATTCGTCCATAACGGTGTGCCCCCTCTGGGAT
ATAGGATGAAATGAATTGATCTGAGTACCTGGGATGTAAAGTTACTAAAA
CGCCAGCTAGGTTACGCCCCGATGCTTAAATATGATCGTGGCCTACACC
TCGTCCAGCAGAAAAAGTACCCTTTCTTCAACACCACCTCAGCATCCTCC
AATTTAGGAGCTATAAACTCATGACTCTTTATTTACCCCTGCAGATTC
TCAATCCCAATAGTGTGTCTCCCTGTGAACTCACGGATATACCGATTTT
CCCCACGTCATTTCCACACGTCGCAATCGCTTAGTCATCCCTATGTATGA
GAATCATGGATGACTATGTTGAAGTCCATCTATAAAGTTCAACCCCCATC
TCCGTCCCTGATTTCCCTCCCAAGATCACCAACGCGACTCGACATATT
GTTATCGCCCCAAGGGACCTTTGCATCCCCCATATCCACTGGTCACCTCC
CCTCTGGCTGGAAGTCACCGGGAAGTTCTCCACATGTTGT

>Contig16

TGCGAGCGATGTTCTTAACTTTAGCGCCATTGACTCGAGCATGGTCATG
GCTGTTTCCTG

>Contig17

AGGGTGTTCCTAAAGGATACTACGTTCCCTAAAGTCCAGAGAAAAA
AAAGTAACATAATGTGGCTTATTTGGTATAAAATTTTACAGGAAGCATT
GTCAAATATGAAATAGTGTGTTGGTTTTGTTGGGCTGTATTTGTATAAAT
ATGTTATTGGTATGTGTTCCAAAATTATAGGAACTCCTATAATTCTGAT

ATGACTTGGTGTACATTATCAGTAATAATTATAATTGTTATGGTAAATTA
TTGTGTGCCATGGAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTA
TGGTTGCCCTAAAACCTTTTGGCCATTACAGACAATTGTCTTGCTTTGGT
CCTCTTTAGAAGGTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCT
CTTGAATGCAGGCTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAG
GAAAAACTTTTCAGTATTCATGGAGTGCTGAAATATTCATGAATATCAAGC
AAAACAGGAATTAACCTTCATAGATGGAATAAAAGAATGCTGAAGTAATC
TTTTTGACTTTTTTTCTTAAATGTTGATCCTTCGTTTTGTTTTTCAGAG
TCAAGGAAATTTTTCTGTTGAGATATTGACAGCTTTTAACAATTAAGTAT
ACTCCAGTGAACACAATTTGGAGCATATTTGTGTCTCTCTATATATATTT
GGAAACAATNTTTGAGTATTCTTAACCTATTGCAATATT

>Contig18

GGTTGTCTGTATACCAGTAATGGGATTGCTGGGTCAAATGGTATTTCTG
GTTCCAGATCCTTGAGGAATTGCCACACTGTCTTCCACAATGGTTGAACT
AACTGACACTCCCAACACAGTGTAAGCATTCTCTATTTCTCCACATCC
TCTCCAGCATCTGTTGTTTCTTGACTTTTTAATAATCGCCATTCTAAGT
GCATGAGATGGTATCTCATTTGTGGTTTTCAATTTGCATTTCTCTAATGACC
AGTGATGATGAGCTTTTTTTCATGTTTGTGGCCACATAAATGTCTTCTT
CTGAGATGTGCTGTCTTATATCTTTTGGCCACTTTTTGATGGGTTTTTTT
TTCTTGCAAAATTTGTTTAAATTCCTGTAGATTCTGGATATTAGCCCTTT
GTCAGATGGATAGATTGAAAAATTTTCTCTATTCTGTAGGTTGCCTGT
TCACTCTGACAAATAGTTTCTTTTGTGTGCGAGAAGCTTTTCAGTTTAAAT
AGATCCCATTTGTCAATTTGGCTTTTGTGCAATTTGCTTTTGGTGTCTAA
TCATGAAGTCTTTGCTCATGCCATATGCTCTGAATGGTATTGCCTAGGTTT
TCTTCTATGGTTTTTTATGGTTTTTAGGTCTTATGTTTAAATCCTTCTTTTT
TTTTTTTTTTTTTTTGTAGATGGAGTCTTAGTCTGTTGCCAGGCTGGA
GAGCGAGTGGCGTGTCTNTAGGACGC

>Contig19

GCATGTTGTCTAAAGGTTTGTCTTCTCCAAAATTCATATGTTAAACCT
AGCCCCAAATGTGATAATATTTGGAGGAAGGCTCTTTGGGAGGCAGAGCC
CTCATGAATGGGATTAGTAGCCTTATAAAAGAGACCCCTGAGGGCTCCCT
TGTCCCCTCCACCGTGTAAAGGATGCAACAAGAAAGTATGGTCTATGATCC
AAAAAGCAGACCCCTTGCCAGGTACCCAATATGCTGGCACTTGAACCTCCC
AGCCTCCAGAACTGTGAGAAATAAATTTCTATTTTTCATAAGCCACCGAG
TCTATGGTATTTTGTATAGGAGCACAACAGACTGATGTGCCACCCAAC
CATGATTATACGTGTAATTTATGGTTTTCTCTGCTAGTAGGGATGCACCAT
GGGGTTAGGAACACGCTTTTCTTATTTCCACACAGTCCTTAGCTCTAA
GCATGTTCTGTAATCAAAGATCCCCATCTTTTATGAATGAAGGAGTCAGT
GAATGAATTAATGAAAGAACTGATAACCCCTCAATAATTATTCCAGCCTTT
TATACCTACTATTAA

>Contig20

ACGGTTCTCTAAAGACTTTCAAGAGCTGGATTTTATGCTTTAGGTGAAGG
TGATAAAGTAAAGTGCTTTCACTGTGGAGGGGGGCTAACTGATTGGAAGC
CCAGCGAAGACCCCTTGGAACAACATGATAAATGGCATCCAGGGTGTA
TATCTGTTAGAACAGAAGACAGAAAATATATAAACAATATTCAATTTATC
CCATTCACTTGAGGAGTGTCTGGTAAGAACTGCTGAAAAACGCCATCAC
TAAGTAGAAAAATTGATACCATCTTCCATAATCCTATGGTACAAGAAGCT
ATATGAATGGGGTTTCAGTTTCAAAGACATTAAGAAAAATAATGGAGGAAAA
AATTCAGACATCTGGGAGCAACTGTAAATCACTTGAGGTTCTGATTGCAG
ATCCAGTGAAGGCTCAGAAAGACAGTACACAAGACGAATCAAGTCAGACT
TCATTGCGAAGAGAGATTAGTACTGAAGAGCAGCTAAGACACCTGCAAGA
GGAGAAGCTTTGCAAAATCTGTATGGATAGAAATATTGCTGTCTGTTTTA
TTCCTTGTGGACATCCAGTCACTCGTAAACAATGTGCTGAAGTGGTTGAC
AAATGTCTCAAGTGGTACGCAGTCATTCTTTCAAGCAAAAAATTTTAT
GTCTTAATCTAACGCTATAGTAGGCATATTATGTTTCGTATTATCCTGATT
GAATGTGTGATGTGAAGTGAATTAAGTAATCAGGATTGAATTCATTAG
CATTTGGTACCAAGTAGGAAAAAAAATGTAAAGCCAGTGCTTAGACACA
GC

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CGCTGTCTTAAGAACTGGGCTAGGAGTGAGCAGTGAGCCAAGATCGCACC

FIG. 4 (5 of 61)

59/118

ATTGCACTTCAGCCTGGGCAACAAGAGCAAACTCCATCTCAAAAAATA
CATATATATATATGACCCATAAAAAGGAGATAAATCAACACTTCAGAACT
GACCCAACTTGCAAAGATACTATAATTAACAGAAAAGGACAGTTTACTA
AGTACTCCGTATGTTCAACAAGTGAAAGATTAAACATATTAAGTAGAGAT
GTAGAAGATATAAGAAGATCCAAAATGAACCTTTAGAGTTGAAAACCTACA
ATATTTAAGATAAAAAATACACTAGGTGGGATTAAAAGTAGATTACACATT
GCATAAGATAAAAAAAATGAGCCTGAATACAGCACAGTATAAACTATCT
TAAACAAAAACACAGAGAGAAAAATAACTTTAGAGACTTAGCTCTTATC
CTCTATTTGTTTCTAAACAGAGGATAAGGGGCAGAAAAATGTTTGAAGA
AATCATGATTTTAAATTTCCAACCTGAGATAGGAATAGCACTGGGTAGTC
ACAGGAGGCTGGAAAGACCCAAACAGCAGTTAAAACAGGAACTAGGCAAA
GAAACCAAAGGATAACAGTAACCTAACTAAGGGAGAGAAAACTGACAA
AAGCTGACTTAGGATAACTGAC

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CCTGAATATAAGCCGCAAGTAACCAATTAAATTTGTTTTCCAAAATTGTA
TTAACAATCTATGAAATTTTATCTTGACCATAGCTATAACTCCAGAAG
CCTTTTATAACCTCTATAACCTTTATTAAGGAGTAGGTTAATGCTTCAAG
AAAACCTTGTTAATCTGACACAGGACCCATATGCTGATCTTGCACTAGTG
TGGCTTGGACATCAATGATTATGATTAAATTTATAGAGAAATTGAACCTAT
TTTATCTCTCAAAATTGGCCCTTACAATCTCACACACCCACCTCTTCCAC
TATAGTTTCTGGGCCTTGAGTTGAATAGCTTTAATTTCTGGCTCTGTGTT
TCAAGAATGCAGTTTATTTTGATTGGCATTCTTACCAGTCTGAAGATG
AACCTTTAATTTGCTGTGAGTATTAAAGATTTAGCAGGACTTGTCTTTTA
AGAACCAGGAGTCAAGCCCTATAACTCAATGTCAAGGACTTTAAAAGC
ACATAACATAAAGATATATGGATGTAATAATCATAATTTTAAAAAATTGT
ATTAATCTCAGTGTTTTCTAAGCAAACCAAACTTAATAATAATGGCATA
GAAATTATTTCAATAAAACATAAAATCTGTTAAGCCAGTTACCAAAAGGC
AAAAGAAAAGACCTTCTGCAATGCACAGAATATTATGTTGGAAGAAAACA
TTTCTTTTAGACCTTTAAGAAAACATTGTTAGCATCAGGACACAACAAAC
AGAATCTGAGGGTAAAAAACGTATATGAGCTGAAGGGAGTTGAAGGAGGG
CATTACTATTTCCACCCCTTTTAAAGGGGAGAGAAAACTAAAAACAGCAA
GATGCAATAAAAGCTGAACCTTGGGTAAAAAATAATCTTAAGTCTCTT
ATAATTTATTAAGAGTGAATCAACCCCGTAAGAAAATTTCAATGTTCTAA
CCAATTTTTTAAATATAAAGTAGTTTTTTAACATCAACCCCAATCTCTAGA
AAGACCATTATAATTTCCCTTTAATTATAGACAACCTTTATCATATAAAAG
TTTTTTTAAATAAATCCTCTTATTTGTGACTTACACAGACTATTATGACA
TGCTTGGACTTTCTGGTTTGTGCTGAACATCCTTTTCTTTCTTTCTTCT
TTTTTAAATTTTACTTTACGTTCTGGGATACATGTGAAGAACATGGAGGT
TTATTACGTAGGTGTACATGTGCCATGGTGGTTTGTGCAACCCATTAAAC
CGTCATCTATATTAGGTATTTTTCTTAATGTTATCCCTCCCTTGCCCCC
CACCTCCTGACAGGCCCTGGTGTGGGACATCCCTCCCTGTGTCCATGTG
TTCTCAATGTTCACTCCCACTTATGATTGAGAACTGCAGTGTGTTGTTTT
CTGTTT

>Contig23

GCTAAATATAAGCTATGATAAAACAGTTGGCCCTCTGTATCATGGGTTTC
ACAACCTGTGGATTCAACTAACTGTGGATGAAAAATACTTGGGAAAAAAG
AATGGCTGCATCTGTACTGCACAAGTGCGTGCTTTTATTCTCGTCATTAT
TCCCTAAGCAATACAATATAACAACTATTTATATAGCATTACGCTGTAT
TAGGTATTATAAGTAATCTAGAGATGATTTGAAGTATACAGGAGGATGTG
CTTAGGTTACATGCAATATTATGCCACTTTATATAAGGCCCTTGAGCCT
CCTCAGATTTTGGTATCCATGGCAGTCTGGAGTCAATCTCCTGCAACA
TCTCCATTGTTGAGATTCTCTTCTATATCATGTTTATATCAGAAAATCT
ACATAAGATTTTTTAAATGTGTTTCAATATAGGTTTTGTGTATTTTTGGTTGT
TAATCCCTAGATATATGCAGTATTTATTGCTATTATGAGTAGTGTCTT
TACCATGTATTCTAGTTGGTTATTGCTGACAGAGAAATGTTGCTGGTGT
TCTAAGTTACCTTGTCTTAAACACCTTGCTGAACCTTATTAGTTCTCA
TAGTTTTTAAATTAATCTTTCTTAGTTCTGATAACATAATCTGCAATAAT
GACAAATTTTATATCTTTCTTCCAATGCTTATATCTCTCAGTCTCTTTA
TCCCAAAGTATTTTCCAGGATCTCCACTATAACATTAAATAGTAATAAGA
ATTTCTGTCTTGTACTGATCTTAAGGAGAATAAATTTAAATTTCTCTG

TCAGGTTTTATGCTTGATATAGATTGTGATATATAGCCTTTCACAGGT
AAAAAAAAAATGCTTTCCTAGTAGTCCTAATTTTTTAAAAAATCATCATA
AATAGATGTTGAACATTATCAAATGCTTTTTCTGCATCTATAGAGATAAT
CATATGGTTTTTTACTATTTATTAATGTAATGAATTAGACCAATTTTCTA
ATGCCAACTCTTCTGTATTTGTAGGGTAAATCCTATGGGATCATAAAA
TACTTTTAATACATTGTTAGATTTGAAGAGTTAACGCCTTATTTAGAACG
TTTTCAGTCACATCCATAAGTGAAATGGCACTATAGTGTCTATTACTATT
ATATTTTTCTGGTCTGAAACCAAATTTATACTCACCTCATACAGTAAGT
TGGGCAACTTTGTCTTTTTTCTGAAACAATTTGTGTATAGAAGAAAT
TAACTGTTCTTGAAGTTTGATAATAATCATCCAGAAAATTATCCCAT
CTAGGGCTTTTACAAAAAGGAGACTCTAGAATGCCATTTTCGGTTTCTTG
ATGTGTATTGGCCTCTTTCATTTAGGCTTTTGGATTTTTTAGGGCATT
TTCATATAGGCTTTTTTACCGG

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CATAAACTTCAGGTTGGATGTTCCGTCAAAGTGGTCCGGCGATGCGAAAA
CGAGAGGGCTCGAGGACTGGGCAGAGAACTATTTGAAGGTATCTCTCAGG
GGAAACCAAGCGGAAGGCGGGAGTAAATTTGGAGGGAGCGACGGCCTT
CAAAGAAGGGGCTTGCTTAGATCGGCGAGATCCGGGAGGGTCTGGTGGG
GAGAAATGACTAGAGGACAAATCTAATGGAGAGACAGACGGAGATAGATA
TCGTGACAGAGAGAGGGACAGTGACAGCGCACACAGTGCAGGGTCCATG
AGTACAAGGCCCTTAAGTGACACCCAGCCGGAGTCATGGCAATTCGAT
TCCTGTACTGACCACCCAGGATTTGGGTAGACTGTACGAGTTAATGAGCA
TGGTCCCCAACAAGACTGCTTCGACCTCAGATGCAAAGCACACTTCAGGG
GTCCCCAAGCCACTCATGTTTTTTGAATGACTGCCATAAGTTCAAAAATT
CCCACAATTCTCTCAGATTCAATAACTGGGTATAACCACTCATAGAACTC
AAGAAAATGCTATCATTTATTATTACAATTTTATTATAAAGGATACAAATC
AGAAGGACTAGCCAAATGAGGAGACACATAGAGAGAGGACTAGTAAAAAA
CAGAGCTTCTGCGTCTACCTTCAAGGAATCAGGATGCACCACCTCCCA
GCACATCAAGTGCTCATCAACCAGGAAGTTCTCTGAGCTCCAATGTCCA
GAGATTTTAGGGAGGATTCAATACATAGGTATCATTGATTAAATCATTGG
CCATGTACTTGAATCAATCTCCAGTGTCCCTCTTCTCCCTAGAGGTCTG
AAGGGTTGGCTAATATCATGTGGCTCAAAGCCCCAACTCTAATTACCTTT
TTGGTCTTTTTCAGGGACTAGACCCCATCTGAAGCTATCTACAGGCCCTG
CCATGAGTTAGCTCATTAAACATAACAAAGACACTTATATTACTCAGAAAA
TTCCAACAGTTTTAGAAGCTCCATGTCAGGAACCTGGGACATAGATCAAA
TTCTTTTTTTTTTTTTTTTTTTTTTGGAGACAGGGTCTTGCTGTGTTGCCAG
GCTAGAGTGCAACGACAGATCACAGCTCAATGCAGCTTCAACTTCCAGG
CTTAAGTGACCTTTCCACCTTAACCTTCCAAGTATCTGGGACCAAGAAA
ATGGCTAATTATCTGGCTGATTTTAAACTTTTTTTTTTTGTAGGGATG
GGATCGCCCTGTGTTGCCAAGGTTGGTCTCAAACCTCTGGGTTCAAGCAA
TCATTCTGCCCTGGCTCTGTGATGGTTAATACTGAGTGTCAACTTGATT
GGATTGAAGGATACAAAATAATTTTTTGGGTGTGTCTGTGAAGGTTTCG
CCAAAAGACATTACTTTGAGTCAGTGGACGGGAAATCCCCCTTCCCA
TGGGACGGGGAGACCCCCCTCCATCCAGGTAAAAAATCTAATCACCTGC
AATGTGGCAGAAATAAAGGAGGGAAAAACGGGGACCCCTANATGGGTTA
TTCTCCACCTAATTCTTCCCCCAGG

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CCATGTATTTTCAATTTCTACAGACCCTGAGATGAATTTGTCAATTGCCACGG
GGTCTGAAGTTCAAATACTCTATTTGGTATCCTGCCCCCTGTGGTTAACT
GTGATCATTTCACTCACCTTGTTTATGATGAGAGGTGCCACCATCTGGCC
TCCTCCACTCTGCAATCCTGTTAATTCCTATCAAAGCTGAAAACCTGCTG
CAGCACCCACACCATCACCTCCAGCCTAGAGAGGGAAGCTACCAGTGAGC
TCTCCTGGATGCCGGTGTGCCCCCTCGCCAATACATTTCTTCTAGTCCCT
TGGTCATCCTGAGGTGTGTGATTAATGGACAGCTATGTGGATTGCACATA
ATAGATGTACTCCAGCATCTTCATCCCTGATTTTCTTTACAGAAATCAC
TCAACCTTAGCAACATGTGAAAATCACCTAAGGACATTCTTTAAATCCCT
CTGTCCACATGGCAACACAAACCACTTAAATAAGAATCTCCAGGGAGTCA
CTCAAGCATCAATGTTTTTTAAAGCTCCAATTTAAGGATCATTACATTA
TGTCTGAAGAAATTATAGTATTTACGCTTACTGACTGTAAACCACCACCA
TATCTAAGCATCCATTAGTCAACCTAGCAGACAATAAACTAACATTACCT

FIG. 4 (7 of 61)

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CCAGGTA CTCAAATCAATTCATTGCATCCCAAATCCCAGATGGGCCCCACC
CTTATTGACAAATTCAGCCCAATCTTGGTTGAACACATTTAGAATATATT
TCCATGAACAATATCCGGTTGACGAGTTTCTTTAACTTTTTGGAGTTTAA
GCCATTTCTTTTACAGTAGCCTTGTTAATCCCTGTCAATGCTCCATGG
GGGTCAATGAAGAGACCTCTTATTAAGTGTGAAGCAACTGGCTCAGGTGC
AGACACTCAAATGCTTCACATGCAGTGGGAAAAGAGAGTGATTGTCTAC

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TTTAAAAAGAACTGAGTCTTTATTTCAGTCGATTCTTCTAATCTATGAACA
TAGCATCTCTCTCAAAGCATTTAGTCCTTCTTTAATTTCTGTCAATTAATT
TTTTAAATTTTTCATCCTAAAGATTCTGTATATGTTTTGTTGAATTTATG
CTTAAGCATTTTCACTTTCTTGGTAACAATTATAAATGATTTTGTGTTTTT
TATTCCACTAGTTTCATTTTCAGTGTGTAGAAAAGCAATGAATTTTGTGT
GTTGATCTTTGTTCCAACATCTTGCAACATTATTGAACTCATTATTAGT
TCTAGGAGGTTTTTTCATTTTTCTGTAGATACCTTGAGATTTTCTATAT
AGACAGTCATGTTGTCTGCAACAGGCACAGTTTTATTCTTCTTTTCA
ATCTATATGCCTTTTTTTTTTTTTTGCCTTATTGCAGTGGGTAGAAGTT
CTAGCACTATGTCAAATAGCATTGGTGAAAGCAGACATCCTTGTTCTTG
TCTTAGAGGAACATTTGGTCTTTAATCTTGATTTAAAAAATTCCTTGCAC
TAAGTTACCGTGTTTTGCGGGAGGGAGAGGTGGGGTGAGGTGGGGATTTC
CCCTAATGTTTACAAGCTGGGATTTTCTTTTCTGTGTCTAATTATTTT
CCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTGTATAAAA
TAGAATTAGCCCAAGCATGAGTCTTTATTTCAGAAGAAATTTTCATGGACGT
TGTGCCTACTCTCTTGGCTTCCTGGCTTCATGGCTTCCAGATCCCACAG
TAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAATAAATGA
AGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGGCCTTTAA
GATCCATGAAGTTCTCAAACAAAAGTGATAACGTTATCTCCATGCATATA
TAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAAGAAAGGA
GACCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCATCCCACC
GAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCAAGAAAAG
CCAGAAATCCAGGTTTTTGCCTGAAATGCTGATTTTAAATGTTGGGAAC
TAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAAGTTGTATGTG
GAAGTGTCTTCTCCAGTGGCGACCAAGTTTGGACCGTTGATACTCAGCAA
GTTTCAGCCAAGTGCGCCTTGTCAATTGTCAAGTCAAGGTGATGTGTGAT
TGGTCAAGCAATTAATTTTGCTCAGCATCTCGTGTGTTTTCAAAGAAGT
GAAGGTTCAATTGC

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TTTCAGAGCACAATGCGTATTTCATAGTATATTGACTTAATTTCTAAGTGT
AAGTGAATTAATCATCTGAATTTTTTTATTTTCAGATAGGCTTAACAAATA
GAACATTCTGTATATAAATGTGTAAATTAGAGTTAATCTTTCCAATCACA
TAATTCGTTTTATGTGAAAAAGGAATGAAGTGTTCATGCTGGTGGAAAG
ATAGAGATTATTTTAGAGGTTTGTGCTTGTGTTTTGGGATTCTGTTTTT
TTTTAAATTTGTAAATGTACTTGTGTGAATGATTTTTTAAATGATTT
TACCATTTTTGGAAGGGTATTTAATGATAGAATATCATCGAGCCAACATG
CACTGACATAGAAAGATGTCAAAGATATATTAAGTGTAAATGCAAGAGG
GAAACACTATGTACAGTCTGAGCCAAATCAAAGCATGTATGTTTTTTAT
ATGTGTACAACAAAAGGTTTGGAAAGATATGCGCCGAATTGTAAATGTG
GTTTCACCTGAGGGGGTGGGAGGATGGGGCCCCAGAGGGGTTTTATGGG
GGCCTTTCACTTGGTATTTTTTTTCATTTTGTTCTGTTTGAAATTTTGT
TTTCTTTTTTAAATGGAGTTTCACTCTTGTGCGCTAGGCTGCAATGTAGTG
GCGTGAACTCAGCTCACTGCAACCTCCGCCTCCAGGTTCAAGTGATTCT
CCTGCCTCAGCCTCCCATGCCTCCTGTGTAGCTGGGATTACAGGCACCCA
TCACCATGCCTGGCTAATTTTTGTATTTTCAGTAGAGATGGGGTTTCACC
ATGTTGGCCAGGCTGGTCTGTAAATCCTGACCTCAAGTGATCCACCCACC
TTGGCCTCCCAAAGTGCTGGGATTTCAAGGTGTGAGCCACCACGCCAGCC
CTGTTTTAAATTTTTATAAGTATGTACTACTTTTGTAAATCAGAAATTATTA
GAAAGCATTTTACTGATTTTAAAGCTTAGACATGTTCAAATGCCTGCAAA
ACTACTTAACACTCAGCTTTAGTTTTTCTAATCCAAAAAGCCGGGCAGT
TAATCTTTTTTGGTGCCAATGTGAAATTTAAACGGTTTTATGTTTTTCTG
TGTTGTGAATGAAAAATATTTCTGAGTGGTGGTTTTTTGACAGGTAGACC
ATGTCCTGTCTGTTTTCAAATAAGTATTTCTGATTTTGTAAATGAAAT

ATACAATATGTCACAGATCTTCCAATTAAGTAGTAAGGGTTTATCCTTAA
TCCTTGCTAATTTAAGCTTGCATAAGTCACTTTACTAAAAGATCTTTGTT
AAGCTAGTATTTTAAACATCTGTGACGCTTATGTAGGTAAAAGTAGAAGCA
TGTTTGTACACTGTTGTAGTTATAGTGACAGCTTCCATGTTGAGGTTCT
CATATCACCTTGTATCTTGAAGTTTCATGTGAGTTTACCATTAGGATG
ATTAAGATGTATATAGGACAAAATATTAAGTCTTTCCTTTACCTAAGTTT
GCTTTCTTGACTAGTAATAGTAGTAGATATTTCTGTAATAAATGTTCTCT
CAAGATCCTTAAAATCTCTTGGAAATTATAAAATTATTGGAAAGACAAGA
ACAGTTTTTATTCAATTATATGCATTATTATCG

>Contig28

CTTTCTCAAGAAAAGGGAACCTGGAGCAATTAACATATGTAATTTTTTTT
TAAAAAACCTTAAACCTTAAACATCTACCTATATACAAAATTAATTAACA
ATGGATCATGGACTCCAATGTAAACATGAAACTCTAACTTCTAGAAAA
AAAACCTGGAGAAAACCTTTGGTACCTATGACAAGGCACAGTTTTTAGACT
TAACACTAGAAGTGTGAACATATACAAGAAAAATTAATAATTTGAACCTT
ATGAAAATCAAATTTTGTCTCTCCAAAAGACCCTGTTAAGAGGATGAAA
ACTAAATTACAGATTGAGAGAAAATATTTGTAAATCACATATTTGACAAT
GGACTTGTATCTAAAATATCTAAAGAACTCTCAAACTCAACATTAAAAA
AAATATCTAATTAGAAAATGAGTGAACATTTTACGAAAGGGCCTTATAG
ATTAGCAAATAAAACACTTGAAAAGATACTCAGCATCACTAGCCATTAGA
AAAATGCATATTAACCACAATAATGTATCGCTACACACATATAAGAAT
GGTTTATGAAAAAATAGTGATGACACCAACTGTTAGTGAAGATGTGGAGA
AACACTCATACATTGCTGGTAGAAATGTAAATGGCATAGCCACTGTGGA
AAATTATTTGGCAGTTCTTTTAAACTTAAATCAATCTACCACACAAC
CCAGCAATTTCAATTACAGGGCATATATCCAGAGAAATGAAGATTTATGA
TCACACAAAAATCTGTACACAAATGTTTTATGGTCATTTTATTCATAATA
GCCAAAACCTGGAACTATCCAAATGTCCTTCAATGGGCAAAGGATTAAA
CACACTGTGATACATCCATACCATGGAATACTACTCAGCAATAATAAGGA
AAGAATTACTGCTACACACAAGTTGGATTAACTCAAGGAAATTTGTGCTG
AGTGAAAAATTAACAAGCCAATCTCAAAGGACACATACTTCATGATTCCA
TTTGTATAACATTAAATTAACACAATTAATTACAGAGATGGAGAACAGAAT
AGTGGTTGCCAGGGATTATACATGGTGGACGCGGTGAGGCGGGCCTCCAC
GCCTTGGAGATGAAGGGGGCTACACCCTTTAAAGCACCCACGAGAGAG
TTTTGTGCGGAGGGGGCCCAATTTAAGTACTCCGCCCCGGGGGGGAACAC
AGGGGCAAAACAAAAAAATTTGGCCTTGGGGGTGACCAAAACACAAAAAA
AAAACAAACACACAAAAAAACAACNATGGGTGGGAGGATTAATCGCCAAA
TCTGAGTAAGCTATCTGGACAGTACCAATATCGATTTCCAGTTTTGATG
TTGTACTATAATAATGCAAGATGTTAACATTGGAAGAAGCTGGCTGAAGG
GGGCTCAGGAACCTCTCTGGACATTTCTTTGTACCTTCTGTGAATCCATC
ATTATTACAAAATAGGACATTTTCTAAAGGTTAAATCATTTTAAATTTAA
AATGTCCCTGTTACTGTTGAACTCACATCTCCATATACTGATCAAGAAC
AGCACTAATGGCCCCCTGGCCTCCAGGAATTCACAATTCCTACTGACTTTT
CTTTGAAACCTTGGCCAAGTCGCTTCTCTTCTCTGGTCTCAATTTTTCA
TCTTCAAAATGAAGATTGAATGACTATTAATCTCTTGCAATTCTTGAG
ATGAAGGGTCTTAAAGGAACTGAAGAGGATGCCATGTAATGTAAATATGG
GTTTTTACTCCATCAGCCAGCCAAGACAGAGGGCAGACACCAAGACATGG
TAACCAAGGAGGCCATGTGTAAACAAAGACCATTTAGACTTATGCTCTGG
CCTTTGCAGCCCAACTGGTGTGGCCAGTTGGTGGGGTATGAAGAAAATGG
GGCCTTCCAGGAACCATGTTGAGTGGAGATAAGCAGGGAGGAATGCAGAA
GACATGGGGCAGTGCCAGTCTCAGCCCGAGCCAGCTACCCACACATG
GTTATGAAAGACTGACAGCCTGTAAGNTGAACACAGCCCTGCCTCTCTTA
GATAGGC

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GCAATATGATCTCAGATGTGGATTTACTGTAAAGTTCATCAAATTTAAA
TTTCAGAACACTTAATCTGCAAGAGTCCTTTCCAAGACCCTATACCTAAT
TTTGTGTTTACAATTTTATATTTGTTTCTTAAAGAAGACCACCAATATA
AACTATATCCAGCCTTCATGATAAGTACATAGGAACTATGCAATAAGG
GGGAAAAAAAACAAAGAAAAATACCTAGTTTACTAATGGTTCATCTCTGA
ATAGCACATATTCATAATGATACAAGCACTCATTACTAGTCTAGGAAAAT
GAAGATATAATTGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGT

FIG. 4 (9 of 61)

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GTGGTATAGACTAGGGCAGGACAAAGAACCTAAATCCTCATTTTCTAAAG
ATAATTGTTAATACGTAAAACTCAAAATTCAGGAAGTAACAGTAAAAGCG
GTCATTAAGAAACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGG
AAGAGGGCGACAATCTGATTATTTTGTCAACAAATTTGTAAAACCAT
TGACTGTTTACATGTAGAACTTGGATCTTTTAAAAAACACAAAATAAT
AATACTATTATTTTAACTGGATTTTGAAGAAAGATAAAAGTCTCA
TTTAGTAATTAAGAACTCATTCCAGGTTAGTCCACTCAAACTTATATTC
GAAATTAAGAACTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGG
AGTTTCGAGACCAGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAA
TACAAATTAGCTGGGCGTTGTGCATGCCTGTAATCCCAGCTACTCGGGA
GGCTGAGGCAGGAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAG
CCGAGATCACACCATTCAGCTCCAGCCTGGGCAACAAGAGTGAAGCTCCA
TCTCAAAAAAATAAACTCATTCTTAACTTGTATGTTTGGAAATGTCATG
CAAATATTATTATTTTAACTTGTATGTTTGGAAATGTCATG
ATGAAATTTAGGTTGGGGATGAGAAAAAAGAAAAACATCAACCCAC
AGCCCATTCATTTTCAAGCCGACCCACAGCTCCGGGGAAGGACAGCAGG
TCCATCCTTCACTCTTTCTTACCTCTTCCCTCCTTCTGGCTCTTCCA
CCTCTAATTTGGAGCCCCAAAAAAGGCAGTGGGAAATGGAAAGTCTTTT
GTACGTGGTACTTGCCGGGGAAGCTGCCATGAAAACCTGGCCCCACGGTG
GGGAGGGATGCCCCANCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGT
CCAAACATGTCCGTTGGTCTGACAGGGCAAGCANCANGAAATCATGTATG
AGTATGAAGTATCTGTATGCAAGGCGGGGAGAACACGCGGAGGAATGG
GGCGTGAGAAAACAGCACAGTACGTTTCTTTAGCAGCTGTCTGTCTCAG
CCATGGGAGGTACAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGA
GATGTGAGTGTAAGAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGC
CCTCTTTCTTACCCGAATGCAGAAATGGCCACAGGCCTTAAACACACACA
TGGGTCTCCAGAGAGAGAGGCTCCACAGTGGACACCCGATTCTCCCC
TGGTCAGCAGCAGCAGGCGAGTGCTGGGCCATCATGAAGCTTCAAGGC
AATGAGCTCTCAGCAATAACAGGAACAGTGCCCTGGGGGACTGTAGCTGCA
AGACCGATTTTTCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGG
CTGAGACTAGCTGGCAGCTCCAAGTTGTTGGTCAGAAGAGAACAGGAACT
AGGGAAATTTGGAATTACTGTTACTACAATTCCTTTACATCCGCACAACCA
TGAGGTCCAGCGATTTTCTATTATTTTTTTTTTTAAGACAGGGTCTCAGT
ATGTCGCCCAGCATAGAGTGCAATGATGTGATCATGGTTCAGTACAGTAT
TCACGTCCCAGGCTCAAGTGACCTCCTGCCTCAGCCTCTCAAGTGGCTG
GGACAGCAGTTGCATGCTACCAGGCCAGGCTTTTTTTTTTTTTTTTTTA
GTTTCTGTAGACACATAGC

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GGTTAAACAATGGCACAGGGAAACAAACAGTTCCAGGTGCAGGGGCTCTAA
ATCTATCATAGATGTTAGGTATGGGGGCTCTGCCGACACAACTCAAG
GCTTTATGCTGTTATCTCTTGAGCGAAATCCTGGGAACCTTCGTACATTGC
TTGCTTCAGTACCTTATCAGTTAATCGGACTCTTTGATATGTTGGGAGTC
AGCGTACACAAGTTAACTCCTTGAGGAAGGGGGTGGGTAAGGAGTCTTG
ATGTCTGGTAAATGAAGGAGCGAAATCGAGTTCCTCTGGCTTTCTCAGCT
AAGGGAGAGCTTATTCATGTGGAACAAGGCTAAGTGATTAAGGGAGAAA
GGGAGAGTCTGAAAAAAGGTTAGGTATTACAATGTCAATAAAATTGGTC
TCCTTATACAGTCCATGTTAGTATTCTTTCCATCTTTAATCTCCCTCTA
GCACCACCAGACTTTTCTCTCTGTACCTTGAGATGTAAATTTTGCTATC
TGAATTTTCGTCTAAGAGTTGTTTCTTTAATATGCAAATTTAGGGTTAT
TTAGCTGACAACTGCCAAAGTAGTGAACAAGTTATCAAGAACTTGAACG
TCTAAGGTAGGAAAAAAGTCTTTATGAATCTATAAGATGTACTTCT
ATTGGCATGCCTAATACGTCTATGTATTTACGTGTTGTGTACACAGTTT
TCACTACTGAAAAATATATAGAGGAGTTCTAATTAATTGACTTAAGACAAT
AAAAGCGCTTGAATCAAATACCTTATCAGGAAAAAGGAAAGACAAGTCA
AATGCTTGTTCAGTTTATATAACTTAAGTAAAAATCTTTAATAAATAAGC
TAGCTTTAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG
TTACAGAACTAGTGGGGGTGCAGTGGGGTGAGGGTTGGTGGGGTGGGGG
TGGTACGGGGGCTTTGTTTTTCTTGCTGCCCCCTTCTGGGTTGGGGAAG
TGGCAGGACCTTGGCAGCACCCCGAGCCGGCATGGCGTTAATAATGGAGG
GATGCCAGACCCAAGTGCTAAGGCCCGGCTGCAGAGCCAAGTTGGCATT

FIG. 4 (10 of 61)

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TCCAGACTGGGGCTCGGGCCGCACCCTCTCCAGGACCCCTCCCCTTGTACC
GAGCAGATTGTGCGGGGAGTTTGGGCCAGCTGTCTGGCGTGGAATTTTC
CCAAATTCAACAAATCCTCCAAGAAATCAATCCATCCATTTCATCCATCCA
TCCATCCATCCATCCATCCATCCATCCATCCGTTGGCAGATTATGAAGCAT
GGATCATTACTTTTGGGATGTGGATATATTCAAGTTAACAAGGAGCAGCTT
TCAAGAGCTGGATTATATGCTTTGGGTGAAGTTTAGAAACACTAGCTCCC
AG

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ACCTCATGTGCTCTAGCGCCTCTTACCTCATGCCCTCCACTCTCAGTCTT
GCACTCACCCCTGCCACACTCAAGGGCTTCCCCAGGTTCTTCTTAGATTTC
CACCGATAGCTCAGGGACTTTGCACATGCTACGGTCTCTGCCTGGCTCCT
CCCCAGATCTTCTCATGCCCTAGCTGCTTCTCATCAGCACCCCTCAGAGAC
TGTCCTGCCCCACCTCTCCAGGTTCCATACCTGCCACCCTCCCCCAATC
ACGTAACAGTTTCTTTCACAGAGCGAGTTACCATCCAGTATTTCCCTAAC
TTATTTTTTGTGACTGGTCTGTGCTGTCTCCACCACAAGAACATAAGC
TGCAATGTGAACAGGAGCCTTGTCTATCTTGTCAACCCAGTGCTGTGACA
TAACCTGATACACATTAGATGCTCAATGATGTTTGATGAATGAAGTGCTG
GTAGTCCAACCTGTGTTTCTTGTCTGTGTAAGTATGTCTGTGTGGTTTC
CTAAGAACCTACAGCTCTCCACTGTGACTCCTGTTCTATGGTCTCTGATT
TGCTGGACTAGAATCCTAACCTACATGCTTACTCTTAGTGCTCTCCCCCA
GAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGGCTAAGACCTAGCT
TCCAACCAGACAGGCTACGCTGAGACCTCAGCACCGCCCTTCTGCGGTC
TCATCCTTAAACGCATCCTTCAAGGGCCAGCTTAAATGTCTCTTCTCCAAG
GAAGGCTATCCTCTTCTGCCCCCTCAGTGCTCTCCATGCCTCCTCTATGC
CTCCATGCCTGCTTTCACACCCTGCAGAGGTGGAGAAGTTGCTAATCTGC
TGTGTTGACATGTGCTGGGGTGCCTTGGGCCAGGGAGCAGGCTGGTGGTG
TGCTGATAGCCCGTGGCTGTGCCAGGTCCATGCTCACTTCTGAGCCCC
AGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCAGAGGAAGGACGTG
CTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGAGAGAAGGCCCAGC
CATCCTCTTGCCCTCTTCTTCTCTCTGCCCCGAGTAATAAAGGTGCCT
GGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACCACACATTCCCAGT
TCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAACGCAGAGTCTGTT
TCACACACCCCAACCATCTAGTATTGGATGGGAGGACAGTAGCGTGACACT
CTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCAAACCAGATACCAG
AGGAGCCCTGTACTGGGATGCTATTGGATGCTTGTCCAGTCATGTACAAA
GTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATCTTCTCTGTAGGG
AACCAGAGGGGAGAAGAGATATGTAGTAGGATTTAACCTGCAAATCCT
CTGCTGAGCACCGTGCATACATACAGTGGGTAGCATGTGGTAGGTGCTC
AATAACTATTGACCGATCTATTGAATACACGTAAGATCGTGACACTATCT
AAAACGNGGGGTGTGGGGGAAAAACCCCCCTTGTTTAGGAAACCCAAA
TTGGACCGTGTGGC

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GCGCGATTGTGCTAAAGATCATGCATGCCTGATCAAACGTCCCCATATGG
CGTCTCAGAGTCAACTCCTTCCCCATCAGTGCCCTGACTTCGGCATAACA
AACCTGGCAGGTTAAGTGATTAATCGGTCTGTACAACTGTAGCCCTTAG
CAGGAAGCACTAAGCTTCGTTTTCAATTTATTTCTTCCCTGGAACGTCAAG
AAATGAGGGATGCCTTCCGCCATGAAGTTTGTCTGATTGTCCACTTTGTT
CTCAAGGAGATATTACAGTTTTTAATTTGTCTTTCTCTCTGCTGCTGCTC
TCCAAACCTGTCCAAAGAAGCCAGCTGGCTCCATCATCTGTAAATCACC
ATTGTCAACAGAGCACTTGACTTCTGTTGCCCTACAATCCACCTGCACT
TTATTTCTGCCACCATGATAATGTAGTGTTACTACATTTTACATTACAGC
TGTAAGAAATGTTACATTCAATTTACTTAAATCAAATTAAGTCTGCTCACT
CAGTCCCCCAGTGACCAACTTATAAAGAGAAGGTACATTTCAATCAT
CACTGAGGTTCTCTACCACTGGAAACTGAGGAAGGTCTGGAGTCCA
CAGTGGTTAAACATCAATGCTCTGTTTCTTCTCTCTCAATGTAACCAT
CCAAGTTTACTCAAAATTCACAAAAAGAGGTCTTCACTCTGCTCTCAA
GACCCAGAGGGCTGGGTTCTAAACTCAAAGGCCAATGTTCCCCAATTTT
TGCATTGTTTCAACATTGGGGAAAACTCGAGGGGATTCAAGAAATGGTTAT
ATAAGTTTTGTGAAAAATGTATAATTTTTTAAATTAATAACAAAGTA
TTATGGAAAGCACTAAATATTGAATTTATATAAATATTCCAAATATTTTT

CTAAATTTTGTAGTGAGAACTTGAGCTTGCTTCTGTGAGATATTTATTTT
AAAACAGATTTGACACTTAAAATGTCTAATCAAGCCTTTTAAACCATGAT
CTATCTCTTCAAATTTCTTCAAGATGCCACCATCAATAAAGAACTTTGTTT
ACACAAGTAAGTGGTAGCAAATGGCAGGGTGTATCATTTTTTTTTTTT
CTTTTTTTGAGACGGAGTCTCGCTCTGTGCGCCAGGCTGGAGTGCAGTGG
CGCGATCTCAGCTCACTGCAAGTTCCACCTGCTGGGTTTACGCCCTTCTC
CTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCACCTGCCACCACGCC
CGGCTAATTTTTTGTATTTTTTAGTAGAGACGGGGTTTACCGTGTTAGCC
AGGATGGTCTCGATCTCCTGACCTCGTGATCCGCCCCGCTCGGCCCTCCCA
AAGTGCTGGGATGACAGGCGTGAGCCACCGCCCCCGCGCTGTTTATCA
TTTTTTGCTGATGAAATTTTCTTGCCACTACTCTGGATGGTTTGATAC
ATTTAAATTTGTGCTTCCAGGGTACAATTATCCTTTAAATCTATACCTCTT
TCCTTTCTTTTATTGACAAATATAATGTTACACTTTTCTGTCAATTGCAGC
CACACCACAGTACACAGATCCCAACAGAGTTGTAATATTTTATTAGTTT
CAGAGTTTCAATATTTTATCACTTTCAATACTTCATGTGCAGGAGTTTFA
TTTGGTACTTCTTTACAAAATAAATGATGTGCTTCCAAGCATTCTTTTC
AATAATCCAATCAATGTTATTAAGTGAATACTAGTATCTGTTTATT
CATAAATTCACAGGAAATGCTTTTTTACTTATTAGTCTTTGGAATCTGT
TGTTTGTATAAACATCTTTTATGATGGCTTTGTGTCTACCAATAGCACTA
TTGCCAAAAGGCACCTTTTTCTTGTCTTCTTACTTCACTGGTCCGAAGCC
TGGTACCAACAACTACCACACAGACTGGGAAATGAGCAATTTTGCCACGT
GCCCTTAGCTATTAATGGTGGCACTCCATACTAGCATCTTAAGCTCAAT
TTCATGAAAGAAATGTGTTTCTTATTTTGTACTTGCAGGCACCTTTTAAA
CTTGTAATCTTTTATTCACTTTAAAATTAAGACAGAGTAATAGAACCC
ATAGAAGGAAATCAATACCCACGAGTCCATACTGATATAAATAAATAGTT
ACATAAATAAATGGGGGGAGAAATAACAGCTCTTCTTACAGAAAAATTT
CAATTAATAAATGAAGAAGGAAATAGGGAAATACAACGTTACCATTAAGC
AACCACAGTAATAATCATTACAGGCAATATCCAAAAATAAATTCAAAGC
CAGTGGGCAAAAGTTTGAGGAGATACAGGATATTAACATAGTCTCAAAT
AGCTCATGCTATTTATAAATTACAAAAGGAAACATAACAACTGTATAGTG
AAGAACTCAGCAGACACCACCTTAGCCAAGTGATCAAGGTTAACGTCAC
TAGTAATAGGGCTTGTGACATCTGACTCCAATCTGATACACTGATAA
GGACACATGACTTCTGCAGTATTCTTACCAAAAACAGAAATCTAATGTAA
TTAAGGAAATGTGAGACAAACCTATTCTGAGAAACATTCTATAAAACAA
CTAACCAATACTTTCAAATTTGTCAAGGTCAAAAGACCAGGCGATGGTC
ACAGATTTGAGGAGACTAAGGAGATACAACAACTAAATACACAAATGGAA
CCATGGCATTCTTGATTGGATCTTGAAACAGAAAAAGGATATTAGGAAGA
AAAGCTGATGAAATTTCTAATACATTCTGTAGTTTAATTAATAGTATTGTA
CCAATATTAATTTCTAGATTTGATCATTATACTATGGTTAAGTTTTTAA
CATTAGAGGAATCTGGGAGAATGGTATATATGAACCTCCACTGTTCAATCA
ACTTTTTTCAGTAATATTATTTCAAATAAAGTT

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GGGAGCGGCGGCCACGCTGATCTCTAAAGCTTTAGACCACATTGGCTCG
AGCATGGTCATGGCCGTTTCCTG

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GACGTCTTAGCGCTATATTATAAAGAAATATTCACCTCCCTGCTGAGCTT
ACAGGGTGACCTAATGTCCAACAATATGAAATCTCTTCAATGAATTGCA
GCACGTCCATATATAACCCACATGGAAGCTGTCTCTTTCTCACCTTCG
AACTTCCCATGCCAAAGAGGGACCTCTTGGACTCAAATACATCTTAGCAA
TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTTACAGTGT
AGCCCCACAGAAAAACAATATGACCCCATCAGTCACTTGTCCCTTTTTT
CCATGCCTCAGTCTAGTCAGGAAACCACTAGATCCTGGATGGCTTCTTCT
CCCTTCCCCTCTTTCTCTCTCTCTCCCTCCCTTGCTCCTCCTTCTC
CATCACCCTCCTTACTTCCAACCAAACTTGACTAGCTCCAGTCTCAT
CCCTCCTTATTGAAAATATTTTACTCAGCCCTCCTCCCCACTCCTGCC
CAATCTTTATTCTTACCTACATCAGACTTCACCAAAACAAAGGCCAGGA
TAATAAACAGGACAAACTCTTTCAAACACATTTAATGACCATATTTTGT
TATTTTGGTACAATTTGAGGAGTCCCAATCCCAGGGAAGACTAACAAGA
AGTTCTCTTAACAAAGGTGGGTCTCCCTTACTAAAAACTCCTGTAATGG
CTGAAAAGAGCATGAGGTTTTCTGCATATCATTACACATTCAATAGAACG

FIG. 4 (12 of 61)

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TCATGCAGCTGTTAAAAAAGATCTGTAGAGGCTATCTTGTGACAGAAAG
GCATTGGAGATATACTGTTAGTGACAAAAATAGGTTATAAATGAATTTTT
CCATGCATGCCCTCTATATTTATAAATACACACACATAAAAGACAGGAAGG
ACAGACATTAACATTATAGTGCTTAAGATGATGCATAGTATAATAGTT
AGGACCATGGCCTTTGGGACAGAAACTACAGCCTCTCTCCCACTTATCA
GCCATGGGACCTTTGGGCAATTTGCTCAGCCTCAAAGCCCCCTGTTCTTTA
TCTGTGTGCTGGGGTTGTTGTAAGAGTTAAGTGCAATACACAGAGAGAGA
GAGAGTACCTAACATGTATTATGTGCTCAGTCAATATGCATCATAGTACT
CATTGTTACATATGTTTCTAAGTGCTTTATACGTTTTTCCCTAAGTTGA
CCATCTGTTTTTGGCATTATGAAACATAATGATCCTAACAAATTAAAAAT
AAAAACATAAAGAATATTTGCCCCAAAAAAATAAAGAACATGAATTCCTC
AAGTAGCCCAAGGGGCATAGACAGAAAGTAAGCCCTTGGTGGGGCTTAGTT
GAGAGAAGTCTCCAGAAGGTCTTTCGTGTGTTAAAGAAGAGGGTAACAGG
GAGGAGGTGGGGAGAGATGTTAACTGAGTCTAAATGAGCACCTGGAAGAA
GAGATGGGACAGGCCACTTCTGCCTGGACTCCCTGATTGTTAAGAAGAAT
GAAAAAGAGCAGAAGTCTTCCCTGAGCCCACTTCACTCCCTGACTTAAC
CTAGTCTTTGCCCCCTCCCTCTCACTCATGGCTACTTTCTGTGGTCACCT
TGTTGTAGAAATGGATGTGACAGCCACCTCATTTTTTCTACCTCCTTCA
ATGTTTTTAGATAATTTAATGTAGTAGAAGACGGTTACAGCAAAAAATTAC
AAAAATCAAAATATCTCTGCTATCTACTGTTGCATTTCTAACCATCCCAA
AACAGTAGCTGAAAACAGCACTCGTGGTCGAGCGCGGTGACTCATGCCTT
TAATTCAGATACTCCGGAGGCTGAGGCAAGAGAATCACTTGAACCCGGA
AGGTGGAGGTTGCACTGACTCAAGATCATGCCACTGCACTCCAGCCTGGG
TGACACAGTGAGACTCCGTCTCAAAAAAAGCACTCGTG
TATTTTGTTCAGATCTGTGGTTTGGGCAGGGCAGGGCTCAATGAGGACA
TCTCGTCTCCGTTCCCGCAGTGTGAGGAAGTGAAGTGAAGTGAAGTGAAGT
CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAATGGTGCTTACAAT
GACAGGGAGCTGTTGACCAAGGGCCCCAATTCCTCTTCTATGGCCCCCT
CTCGGGCTGCATGGGCTTCTTTACAGAAATGGCAGCTGGATTCCAAGAGCA
AGTATCACAACTACAGAAGAGTGGAGGAATATTGAAAGTTCACAGTCTC
TTAAGACGTTGGCCAGAACTGGCAAAAGCTTCATTTCTGCCATGTTCT
ATTGATCAGTCACAGAACTGCACCAATTCAGAGGAGAACATATAGAGG
ACATCTCTCAATGGGATAAGTGTCAACAAATTTGCATCTATCAAACTG
TCTTTTGGGTACAACTATTTCTATTCCTCCATTATGCAAAATATACTCA
CAACCTCCCAGGGGTGCAAAAGCCTCATCCATTTATGGCAAATGTGGCC
CTTTTAATTTATATAAAATAATTTGCGGGGGCTTCTTTATATTTTTAAC
TCCCCTGC
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GTGCAGAGAAGTGATTTAAAGCCCTTCAGAAAGAATGCTTTATTCCCGTG
GAATTTGGTAACCTTGCTTGGGTGTGGGGAGGTTTGTGAGCTTTCTCCACT
CAAATTATCAGACCCTTTCCATTTAGTGGTAGACATTTCCCTCGTCCAG
GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTTACCCAGGGAGAGA
ACTTGGCTCTAAACCTGTAATAGAAAGGTGAGTTCTGGTCTGGAGGGTCA
ATTTTGATCTTTGGCTCAGATCCAGGAATTGGAACCAAGGCTTTTGAACA
TTTTAATGCAGGGGATTAAAAAATGATACGAGTCATTACGAATATATT
TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAATAAGAACAA
AAATCTAATAAAACAAAATTTGTTAAACACATTTACCAAATTTTTTTTTT
TGGTAAAAATTCAAATGTCAATAAATAAGCTAAAGTTCCTCTTGATGACT
CGCTCCTCTGCCCTATTCCACTCCAAGTAACCACTATTATCAGTCTTGCC
AATACCCCTCCAGACCTCTCTACCTCTATATACCATTAGAAGCATGGT
TTTGCAATTGAGGATGTGAGTGTGTTTGTGTTTACGTAAATGTTATCACTCT
GTTCTTGTTCATAATTTGCCTTTTTCTCTCAATGATTGCTTGGCTATC
TTTCTATTTCACTAGCATCTCCTTTCTTTTAACTTACCATTGTTTATTT
AACCTTGCCTCTATCAACAGATATGTAGGTTGTTTCTAGTTGATTTCATT
AAGTATTTATAACAACGCATCAGTAGATGTCCATAAATTTCTTTACGGA
AGATGGCAAGTAGTGAATTTGCTGAGCCAAAGAACATGTTTAAAAAACC
AAAAAACTAGACGCTACCAATTTTCTCTCAAAATGGCCATACCCACTT
ACCCATACAGAGATGATTTGGAATCTGGCTTCTCACAAGGTGAGATGCC
TTCACAGTTTCATTCTTCTGGCATGTCTTCCCTTTTGTATCTGAGAGAG
CTGGCAGAATGTGTCACTAAATCAAGGATAGAGGGTCAAATGACAGCTC

FIG. 4 (13 of 61)

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AAGCTCACAGGCACCTCTGCTTTCTTCLAGACCACCTGCTTTCTGCLA
 CCAGCTCTGTTCCATCTTATAGAATGGTTGCCACTTGGGTGTCTGCTCCG
 ACAGCCATGTCTATCCTTTGCACTGCAGTTATGAAGCAGACAGAGCTAGGA
 GAGGGGCTTTGCCAGCCTCTGCCCTAGCTTGGAGAACTTCAAAAAAGGAG
 GGTATTGAAGTTGAACTCCCCCAAAAAGGGGTGGTCCCCACACCTCAAAA
 AGTGGTGCCTCCGAAAGAAATGTAAAATTCGTGTGGGGGGGGAAAAAGGT
 TAJTTAGAAATTGTTGGCTTGTCTGTGCCGAAAGTATGTGTGGTTACGGGG
 AGTACCGAAATTCGAGGGGTGGGGCGAGGCCGTGTGTCTTTAGCCCCG
 GGGTTTTTCCCGTCGATGTTTAAGGGGGGGGAAGAGGGGGGATGTTTTCT
 TTCCGCGAAGGTTTTTGAAGAACGGCGTGG

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CCCCCACCAGCCACTACTCAACCGGCCGTTACGAAACAACCTCGCCACAT
 CCACTAACCCGCTGGCTCACCACCCACCGCCCTCCCGATCCCCCAATCC
 AAACCTCAACCCCAACCAAGCGCCTCCCCCTCCCCCACCCTCCAGCT
 CAGCCCCAACCTACCACCAACCCGACTCGCCCAACGAAACCAACAGCA
 AACCCAAATGCCCAACAAACAGTGTCCAAACCCCTCCTTCCCATCAGTTT
 GGTGGGCCCCATCACCCTTCCCCCTGGCCCCAGGCTCTCCTTTTGTGCGCTT
 GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTG
 TTGTGTTTCATCACTGTGAGAAATCTTCTGCATCCCCCTCACTACTCTGCTGA
 AAACACTCTAGTGGTTCCTCATTTGCTCATTAAATGAAAGTCTAGATATTAA
 ACGTAGAAGGCCCAGCACAAATTTGCCCTATGCCACCTACCTCTCTAATC
 TTTTCTCCTTACTCTGACAGACTCTCCGTCTGTCTATTTATGTATTCTTTT
 ATTGCTCTCTTCTACTTTTAGTATGAACTGGATTATGGATTTTTTTAAC
 ATTGCTTTCAAGTATGGAATAAAGAAATTTTATTTATTTATTTATTTATTT
 ATTTGAGACTGGGTCTCACTCTGTGCCCCAGGCCAGAATGCAATGGTGCA
 GTCATATCTCACTGTAACTTCGAATTCCTAGGCTCAAGCCATCCTCCTGC
 CTCAGCCTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC
 TAATGGAATAAAATATTACAATGCCATAATCTTAATTTTCAAAATTTTAAA
 TTACATTGTACCTAATGCCATGCATTTACTTTTTTTCAGTGGGTCAATAG
 CCTCACTTTGGCAAGGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTTCC
 AAACCTCATCTTTGAAAGACATAAGTGCCTGTAAAGTTGTACCACATTAGG
 TTCTAGGAATTTTTCATCAAAGACTTTATCAGACTATTTTCTCTAAGTT
 GAGAAAGAGCTGGGGGCGAGATATGGCACTGAATGACTGAAGAGAAGGCA
 CTGAAATCAGGCCAGAGGTTGCTGGAAGAGCAATGAGGAACACCAGCAG
 CAATGAGGAGCCGGTGATGATTTTGGCTTCACAGGGAGGTGTGTACCACA
 CCGATTTTATCTCTACGTGGATGAACCAAGCTGTGCGCTCCCTTGTCTC
 CAGGACATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCC
 CGGGGCCCTCATCTGCCCCATCCTGGGTGAACACTGGTCTGGTCAACTGCT
 GGGCGTACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCT
 CACGGCTCGCACTGCAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCC
 TCTTCTGAGCTCTAACTTCATGTAGGCGACTCCTGCCGGTGTGCTTCC
 AGGCCCATCACTTCAAAGCATTTTCCCTCAGAACACCATGTCTTGGC
 TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCGCGGCTCTCACC
 TGGATGACTGCATTCACTTCTCCACATTTGCCCCCTCCTTTGGATGTA
 TATAGATTGTTTTAAATACAAATCTGATGTGCTTGTCTCTCTGCTTGAA
 ACACCTCAAACTGCCCTCAGGATAAACCACTGCCCTTGACATGTTTACA
 GGTGCCCCATGGCCTGGCCCTGCCCATCTCTTTCAGCCTCATCTCATGCC
 CTTGCCCCCTCGCTCTGCGGCTTCTGCCCTCCCTAGCCCTCCTTTAGGTTT
 TCTAACACACCATAGTCTTCTAGTGTGGGGCTCTGCAAGTGCTGTTT
 CCATTGCTGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCAT
 CTGATTAATCCCTACCTTCTCTACTCATGATGTTGCTTTCTCAGGGACTC
 TCTCTGACTTTTTAACTAATCAGGGTCTCCCAAGTATATATCTTCATAG
 CACTCTGTATTACTCCTTTCTTAATGACCACCTGCTGTAGACAGAATGTT
 TGTCTTCTCCAAATCATATGTAAAACCTTCCACCAGAGCGATGATTAG
 AGAAGCCTCCC

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GACTGACATTCAGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAA
 CCATGTCTTTACTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCAC
 ATAATTTCTTCACTTTCTTACTGTTTCTTGTCTGGGCTCTGTCTGCT
 TACTGTCTAATATCTTGGCCCCCTTAAAGTTGCTAATCTTCAAACCTCA

TTCTGTGACTGGGCCCTGGTCCTTG...CATGGGCCTTGAAGATAC1CA
CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTCT
CATTGCGCTCCTCCCTCCTCCACCTAATGGGATTTGCTCATAACCCGTGTG
GGACCCCTCCCATTTCCTCCCAACTGAATACTTATCAAGACAACGCATTGC
CATACTCCCTCGTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCCTCA
TTGAGGATCTGCAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGA
GCATGGCTAGTCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTAT
ACATGCTGGGACAAATAATAAGAAATGACAGCATTATGATAATGCAGG
CTGCAGGAGGCAGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCT
CCAATTCTTTGAATATTGGACTATAGAATATGTGATGGATCTATGCTCAG
GTGGGTTCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG
TCCAAGAGGGAGTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACT
GGCCACACTTGTGTGGAGACCTCCAGAGAACAGAATCTGGGTGGTGCC
ATGTACTTCCAGGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAG
AGGGGAAGGGGCAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGC
CAATCACAGGGCTTCCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCA
AAAAAGGACAATTTCTCCTCCCTTTGCATGAAGACTGAGCAGTTTACC
AGATTCCCAGGGAACACCCCTTCCACTCTGGGTTGAATGTGAGTGAGAGA
CATTGAGCTGGAACACTAGAAAACTATTTCTGAGCCACTCACCTTTAG
CCCTAGAAAGTGTGGATTTGTCTTCATCTTTGCCACAGTAGAGACTGC
TGATAGCATCAGAACTGGGCTCTGGAATTAGACAGATATGGGTACAAAT
CTGAGCTCTCTCACTTATTAGTGTGGGATGTAGAGCAACTTTAAATCC
TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCC
ACCTAATAGGGGTTTTTGAAGATTAAAAAAGTTATTCAATGAACAGCATT
TAGCAAGATTGCTGACCATTTGAGAAAAATAACAAATTGTTTATTATTATG
TTATTATTAAACATCTTTCTGCACCTTCTGACTGGGGGCATCGTATCAT
CAGAAATACTTAGGATGGGATGGATTCTGCTGATGGGCTGAGTCAAGGGTG
CAATAATGGAGGAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGA
GCCCAGCATGGTACAAGGCTGAGCTAGTGTGCTGCAGAGCCTCCTTGGACA
GCCACAGAGCTTGCTCTGGCCCTGGAGGAACCTCTTCTAGCTGGCAGGA
CCAGCCACAACAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTCAGGA
GTTCAATTGGACCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTC
CCTACTGGCAGGTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTG
ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTACTATCAGGGATGGGCG
GGTGGCTGGAAATAGCAAATAAGACAATATGATAACACAGTTAACCACC
ACACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATCCAATGT
AGAGAATAATTTAAGGTGTCACTCTCCCCGCCAATGCCATAAGCACAG
GCCTCTGCCTGGGTTTCTCACTGTGGAATGTCTCTGGTCTCCTCATGC
CCAGAGAGTGGGAAGTACTCTACTTTAACACCGGCTTTCTGTCAATTC
CNTGCAGCCCTCCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCTGCTG
CTGCAGTGTCTTTGACTTGTAGTGGTACCTGCACACAGGTATTGGTGTG
CTTGTCTCACCACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCCT
GTTTGACTCACCTGTGATCCTCCACCTCCCACCTGTAGTGCCTCAAGCA
TTCTGTAGAGCACATGGACGCC

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GACTAATAAGTACTTCATTATTTGGGTATTTTCCAAGAACACATATTGT
AGGAAACCATTCTTTCTAAAAAAAAGTGTCTTTTAAAAAGGTGAATA
ATTTTTGTCTAATTCAAAGTTTATTGAAAAGTTATGTATAAAACAAGGTA
AAAGGAACAAGGAAATAAGGGAAATGTAAAGAAAATTATAGAAATAAAGT
GGTATTTTTTGGTAAGAAAGCTTAAAGAGAAATAATTTTAGGTAAGAAAG
AATCTTACCTAAAAATTTTGTGCTAGAATAAAGTGAAGTGGCTAAGAAAGGG
ATGTTCAAAGCTATTTATGACAAACCCACAGCCAATATCATACTGAATGG
GCAAAAGCTGGAAACATTCCCTTTGAGAACTGGCACAAGACAAGGATGTC
CTCTCTCACCCTCCTATTCAACATAGTATCGGAAGTTCTGGCCAGGGCA
ATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAATAGGAAGAGAGGAAGT
CAAATTTTCTCCGTTTGCAGATGCATGATTGCATATTTAGAAAACCCCAT
CATTTAGCCCCAAAACCTCCTTAAGCTGATAAGCAACTTCAGCAAAGTCT
CAGGATACAAAATCAATGTGCAAAAATCACAGGCATTCTATACACCAAT
AATAGACTAACAGAGAGCCAAATCATGAGTGAAGTCCCATTCACAATTGC
TACAAAGAGAATAAAATACCTGGGAATACAACCTACAATGGACATGAAAG

FIG. 4 (15 of 61)

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ACCTTTTCAGGGTGAAC...GCAAACCAC...CTCAAGGAAATAAGAGAGG...A
ACAAACAAATGGAAAAACATTCCATGCTTATGGATAGGAAGAATCAATAT
CGTGAAGTGGCCATACTGCCCAAGTAATTTATAGATTCAATGCTATCCC
CATCAAGCTACCATTGACTTTCTTCACAGAATTAGAAAAAATAATAGCC
AAGACAATCCTAAGCAAAAAGAACAAAGCTGGAGGCATTCTGCTACCTGA
CTTCAAACATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT
ACCAAAACAGATATATAGACCAAAAGAACAGAACAGAGGCCTCAGATATA
ACACCACACATCTACAACCATCTGATCTTTGACAAACCTAACAAAAATAA
GCAATGGGGAAAAATAATTCCCTATTTAATAAATGATGTTGGGAAAACTGG
TTAGCCATATGCTGAAAACCTGAAACTGGACCCCTTCTTACAACCTTATAC
AAAAATCAACTCAAGATGGATTAAAGATTTAAACATGGCTGGGCATGGTG
GCTCAGCCTGTAAATCCCAGCACTTTGGGAGGCCGAGATGGGTGGATCAT
GAGGTGAGGAGATGGAGACCATCTGACTAACACAGTGAAACCCCTGTCTC
TACTAAAAAATACAAAAAATTAGCTGGGCATGGTGGTGGGCGCCTGTAAAT
CCCAGCTACTTGGGAAGCTAAGGCAGGAGAATGGTGTGAACCCAGGAAGT
GGAGGTTGCAGTGAGCCAAGATCACGCCACTGCACTCTAGCCTGGGCAAC
AGAGTGAGACTCCATCTCAATAAATAAATAAATATGGAACCTCTCCCAACA
CAATAATAAGACAAACCCCAATGTTTTAAATGGGCAAAAAATATTGAA
CAGACACTTCACAAAAGAGGATATGTAAATGGTCAAAAAGCACATGAAAA
GATGTTCAACACCATTGGTTCATCAGGGCAAAGAAAAGTAGAACCAATG
AGATGCCTCTGTACACCACTTAAATGTCCAAATTAAAGAAAAAAGTTTT
GGCAAGTTGTGGAGCAACTGAAATGCTCGTGTATTGCTGGTAGAAAAAC
AAAAATGGCATAACCATCGCAGATAATTTGTTGTGAGTTTCTTACAAAGTT
AAACATATACTTATTGATATGACAGTTCATTCCAAGAGAAATGAAAAACA
TAAGTCCACACAAAGACTTGTACCTGGGTGTTTATGGTAGCTCTATTCTAT
AATTGCCAAAAATCTGGAAACAAATCAAATGTCCATCAGCAATGGAATGGA
TATACAAATTTGTGGTACACATGTACAATAGAAAACCTACTCTGCAATGGAG
AGAAATTAACCATTTGACAAACACAAAAACATGGACAAACCTCAAAAAACAT
TATGCTGAGCAAAAGAGCCAGACACAAAGACTGCTCAGCGCATGATTC
CATTCATATGAAATCACAGAAAGGGTCAGTTGAAGGTGCAGAGACAAAAA
GTAGATCTGCAGTTGCCCTGGGGATGGGGTGGGAGGTTGACTGCTCTGACG
CGTAAGGAAATTTGGGGGTAGGTGGGGGATGGTGGGAATATTTTTTGAAT
TGAATTTGGGTAATAGTTTTAATAGGTAAAATATTGGACCCACAGTATTT
GAGATAGGTTTCAGTCAATTTAGACAGTTTATTTTGCCAAGGTTAAGGAT
GCATCCGTGACCCAGCCTCAGGAGGTCTGACAACCTGTGCTGAAGGCAG
TCAACATACAGCTTGCTTTTATTCTATTAGGGAGACATAATACATCAAT
CAATGCATGTAAGGTTTACATTGGTTCAATCTGGAAAGGTGAGGGAACTT
GAAGCAGGGAGCTTCCAGGTTACAAGGTAGATTATTCTCAACAGAAAGGA
ATGCTCTGGTTATGATAAGCGGTTGTGGAGACCAAGGTTTATCTTGTAG
ATGAAGCCTCCGGGTAGCAAGCTTCAGAGGGAATAGATTGTCAAAGTTTC
CTATCAGACATAAGGTCTGTGTTGATGTTAATGCTGGTCAGCTTTTCCTG
AATTCCAAAAGGGAGAGGGGTATACTGGGGCATGTCCAACCTTCCCTTCC
ATCATGACCTGAACTAGTTTTTTTTCAGGTTAACTTTGGAATGCTCTTGGCC
AAGAAGAGGGGTCCATTGAGATGGTTGGGGGGGCTTAGAATTTTATTTTT
GGTTTACAGTGAAGACTTTTCAAGCTAGACACTTAAATGAGTATGTTGCA
AAATGGCAATTTCTTAGCACGGC

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GACGTCCTAAAGAAATGCTAAGGTAACCTCAATTAACCTATGCTAGAAAAGA
GAGTTAAGTATTTAGGAGGATTTAATATGGTGTAAAGTTGTGAAAATCA
AAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAGCCAGGGAAG
GCCATGAAGAAAGAGTTCTCACACTTGATCCCTGATCATGAAAAAGACT
CTGCAAAAAACAAAAACCTTGCAAAAGGCCATTGCAACCTTACACAAAAA
ATACTACTTTAAAAGGACATGTGCCCAGCAACTGCCTGTCCAACCTCAGA
CTGGCAATATCTTTGTTATTGATCTTAGTAGCCAGCATAACTATTTCAA
AACAGTGATGTAATGCTCATTTTTTTTTCTTTGAAAACCTTTGTCTTCCT
GTAAAAACCTTTGTCTTCTTTACTTACCCTGAATATGCACAGAGTTTACT
ATGGAGTGCATATTCCTGTTGCAATGCTCTATTCCCAACAAACATCATT
TTCTTTTAGAGAGCCTCTCTCTGTTTGTGATTTAGGTTGGTGATGTAAAG
CAATGGCATAACTGAACACTGATTCAAAGAAAAGTGGCTTTTCTCTTGT
TGTATTAAGAAGAGGCCTTATAAATAGGATAGTAAGATTTGTAAGTTGAA

FIG. 4 (16 of 61)

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CTTAAAGCATGAAGAAAATTTAGGGGCCAGGCAGGGTGGCTCACACCTGT
AATCCCAGCACTTTGGGAGGCCAAGACAGGAGGATTGCTTGAGCCAGGA
GTTCAAGACCAGTCTGGTCAACACAGACCTCATCTTTACTAAAAATAAAA
AAATTAGGCCAGGTGCAGTGGCTCATGCCTGTAATCCCAGCACTTTGGGA
GGCCAAGGCGGGAGGATCACTTGAGGTCAGGAGTTCGTGACCAGCCTGGT
CAACACGATGAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGG
TGTGGTGGCGGGCACCTGCAATCCCAGCTACTCGGGAGGCTTCAGGCAGG
GGAATCACTTGAACTGGGAGGCGGACATTGCAGTGAGCTGAGATAGTCC
CACTGCACCTCCAGCCTGGGCGACTCAGCAAGACTCTGCCTCAAAAAAAA
AAAAAAAATTAGTCAGGTGTGGTAGCACACAGCTGTGGTCCCAGCTACTC
GGGAGGCTGAGGTGGGAGGATCATCTGAGCCCAGGAGGTCAAGGCTGCGG
TAAGAGCTGAGATTGTACTACTGCATTCCAGCAGGGGCTACAAAGTGAGA
CCCTGTCTCAAAAAAGAAAAAGAAAAAGAAAATTATGTTTTTAAATTTA
TAATTATAATAAATTTAATTACATAAATTTAAGCTCAAGTAATTGTAAAT
ATTCTTTCTGTGCACATAAGTTATTCTTGTATTGACCCACAGGAGCTGG
CCATTCTTCAAGTCAGAAGGCCTGAGAGAGGAGCTGCCAGSTGGTCTTC
ATGGGGCTGTGCGGCCAGTCATCCCCACAGTTGACAATCCTTGTGTAC
TTCATCCTCGTTGGATCCTCTGTATCCCTGACGATGAGCAACTGTGAGGC
CCGTTTCAGCACTGAGTTCCAGTCAGGAAAAATCCACCCACCCACCACA
CGCTCACACTTACACACACATTACACATGCACACACGTTCTGGCTCCGA
AAAAGAAAAAAGCAATTTAAATAATTCTGATCCTTTGCTTATTT
CCACAACTCCATGAAAATTGTACATTGTCCAAGCAACATTTCTTAATAT
TCTCTTTTCTCTCATATCCATTTTCTTACTGCTGTCTCCACCTTTCTC
TTCCAACTCCCTGTTAAATCCCTGCCCCAGCGAATTTTATTCAATTT
TGTGGAATGGAGGCTGCTGTGATTTAAATTAATAAAAAAAAAAAAAATCCC
TACTCCATGTCCCAGATCCCTAGTTGTTTTTTGTTTTTTGTTTTCTGAG
ACAGGGTCTTGTGTCTTCCATGCTGGAGTGCACTGGCATGATCATGGCTC
ACTGCAGCCTCAACCTCCTGGGCTCAAGTAAATCTCTTGGCTCAGCCCTC
CCCAGTAGCTGGGAGTTCAAGTATGTGCTACCATGCCTAGCTAATTTTTT
TCTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAGGCTGGTATA
GAACCCCTGGGCTTAAAGTGATCCTCCTGCTCGGCTTCCCAAAGTGCTGG
GATTACAAGTGTGAGGCACTGCACCCAGGCTGGATCCCTGCATTTTACA
GATTTAGCATCACAAAGTCTAAACAATTAGACTGACTAAGGCAGAACTG
CCCTTATGACAGCAGACATAAGAAGGAAAAGGCCAAAAACACTGTGTTAAA
AATTATCCAAATGTGAGGAAAAGGCCAAAGAGAGTAGGTGTGCCTTTTATG
TGTCTAAGCTGCCTGCCAAGGGGCATCTGATGCTCTCAGGCAGGAGTCC
ACAAATTTTTTTTGTAAAAGATCAGATAGTAAATCTTTTCAAGCTGAAG
AGCATGAGGTCTCTGTGCAAAATACTCAACCACCATTAACATGAAAGC
AGCCAACAGACAAACATGACAAATGAGTGTGGCTGTGTCCAGTAAATC
TTGATTACAAAAACAGGCAAGAGGCCAGAGCTGACCCATGGGCCATAGTT
TGCTGACCCCTTCTGTAAAGGAAAGTATTTTGTGTTGACTTGCTGTTTAC
CATTGATTGAACACAAGGCTCTGTAGAGTTACTTGTAACTTGCAAGAAGA
TTGATGAGTGGCAAGTAATTTTTATTACCAGAATATANNATTATTCTGT
TCAGTAGATAAGATAAAACCCACTGTTATATTACTGTCTTGTGTTAGAAATG
GACTTTTGATTCAATTTTTTACAAATTCATATTATTGCCCTAATTTGTATA
TAAGTATGCTTCTTTTAAAAATATATATTTTTTAATAAATTTGAGACAGG
GTCTCACTAGGTTGCCAGCCTTTTGCTATAATGAGAGCATAAAGTGAAT
TTCACACTTTAGCCTAGTGATAGATGGGATTACAGGCACAAACCACTGC
ATGCAGCTAACTTTGCTTCTCATTCAGCACGTTCTATTCCNNNGNTTTT
CATATACGCGTCTCTTAATGC

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CGCATTTCAGCCCAAGTTTTCTTCAGTGTTAAGGTTTTGTGTTACTCTGTGC
CCAAATGTCTTCCAAAAAGGTTAAGTTTTTTTACCTTCTGCCAACATT
ATATGAAAGTGTCCACTTTTGTAGACTTTTACCAATGCTGACTACTTTG
GTTTCAAAAAAGCTCTCAGTAATTTTCTATTAAATTACTTTTACCTTTTT
TATTGAGGGTGTTCACCTTTTTATTGTTAGCATATTCTCTCTGGGCTCCA
TTGGACGCCCTTGGCAGCTTTTTGGTAGTAGGTGCCTTTAGAAAAGTCCTT
CTCGTCTGGCCCTTTCTGAGCAAATCTAGTGAACAGAATTGGCTCCATGC
TCAGCATTTGCTTAATACGGTTGATCCAGGGCTTAGGACTCATTCTTCAT
TACCATCCACTTGCATTGTCTTAAAGCAAGGCTCTATTAATTTAATTTGG

FIG. 4 (17 of 61)

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CATTTCTGTGCCAGCTCTTAGTTCATTAAACAAAGGCTTTAGAAAA
TCCCAGTAGATGCCTATGTTGCTTCCTTTTAAAAAATTTTGGAGCTGTTT
CCCTAGCCTAACCTTTTCTCAGGGCAGGAGTTAAGTCCCTTCTACTGCA
TTCTGTGAAGATGGTGATTCAAGAGGCAGGGCACCTGTTGCTTTGTGAA
ACAGTCCACTCTGCAGCTGGGCAGCTCTGTTACTAGAAATGTTCTCCCTTC
TGGGGAGCCAATATTTTGATGTCCTCTGTGAATCTCATCTGCTTATCCCA
TCTGTTTATGTCCTTGAAGATGCACAGGTCTGACACCACGAGGTAGCCCT
TAGAAATTTGATGGCATTCTGATGTGTCCTCACTCTTCTCCAACCACT
CCTCCCAGAGCTTGTCTTAAGCCCTTGTGGAGCTGATTGCTTTCTCTC
AAGGCAGCTCAGTTTCTTCCAGTTTGCTCCTGGTGGTCTGAAATATGAT
TGACTCCTGAATACTCCAGGTGTGAAGGAGAGTGGGGTGGCCTTTCTAC
TTGTGATGGCCTGGGTTTTAAGTTGCTGTCCAGTGGAGCAGAGGTGACTT
TCCCAGTGAACATACATTTTCTCCCTCTAAATCCTTAGCAATTTTGTCTC
CAGAGGCAAGACCTGGCCAAACCATTTGTGTTGAGGATTGAATCAAGAAT
GATTGAGGAGATGACAGTAGTCCCCCTCATCTGAGGAGGGCGTGTCCA
AGCCCTCAGTGAATTTTCTTAAGCCCTTGTGGAGCTGATTGCTTTCTCTC
CTATGATTTTCTATAAATTAATACATGCCTGTGACAATGTTTAAATTTAT
AAATTAGGCAAAGAGGCCAGGCGCAGTGGCTCAAGCCTGTAATCCAGCA
CTTTAGGAGGCTGAGGCCTCACCTGAGGTGAGGAGTTCGAGACCAGCCTG
ACCAACATGGAGAAACCCCGCTCTACTAAAAATACAAAATTAGCTGGGC
ATGGTGGCAGGCGCTGTAATCCAGCTACTCGGGAGGCTGAGGCAGGAG
AATCACTTGAACCCGGGAGGCGGGATTTGCGGTGAGCTGAGATCGTCTCA
TTGCACTCAGCCTGGGCAACAAGAGTGAACTCCGACTCAAAAAAAAAA
AAAAAATTAGGCAAAGAGAAATTAACAACAATAAGTAATGAAATAGA
ACAATTCTAACAATATACTATAATAAAAGTTGTATGAATGTGGTCTCTTT
CTCAAAATTACCTTTTTTTTTTGTAGACAGGGTCTCACTTTATTGCCCAGG
CTGGAGTGCAGTGGCAGCATCACAGCTTACTGCTGCCTCGACCTCCTGGG
ACCAAGTGATCCTCCCACTTTAGCCTCCTGAGTAGCTGGGACCACAGGCA
TGCACCACTGTATCTGGATAATTTGTTTATTTTTTTTTTGCAGAGAGAGG
AGGTCTCACTATGTTTCCCAGGCTGGTTTTGAATGCCTGGGCCCAAGGGA
TCCTCCTGCCTTGGCCTCCCAAAGTATTGGGATTACAAGCGTGAGCCACC
ATGCCTGCCCCAAATTTATCTTATTGTTCTATACCACTCTTCTTCTTGT
GATGATGTGAGGTGATCCATTGCCTCCTTGATGAGATGAAGTGAGGTGAC
TGATGTGGGCATAGTGATGCAGTGTTAGGCTGATATTGGCCTGATGATA
TGTGAGAAGGAGGTCATCTGCTTCCGTGATCCTGGATCATAGAGTCATG
ATGATGTCAATGGTTGGATGTGAGGAGCAGACGATGTCAATGACTAACGA
TAAGCTGGACAGGTGGGATGGTGGCACAAGATTTTATCACGCTACTCAGA
ATGGAGCACAATTTAAACTTCTGAATTGTTTATTTTTTGGAAATTTTTCAT
TAATATTTTTTGGATTGCAGTTGACTGTGGGTAAGTGAATGTGGAATGT
GAGACTGTGAAAAGTGAGGGAGTACTGTATTATGGAAGTGAATCTAT
TCGGTAGGGGAACAGAAATTCATTTGTGGGGCCAGGTCTCTGCATCTG
TAGGGATCCAATTGTTTCACTTTCTCGTTGTAGCAAAACTTGGCTTTGGA
ATCAGACAGATTGATGTTTGTCTATCACTTAAATGGGTGCAGCTACACTT
TCCTCAAGAGGTAGTTCTGAAAATTTAACAAAATGTGAATTTCTTGGTAA
AAAAAAAAAACCTCAAAATATTCAGTTTCTTTCTTTTGTGTCTGATGT
ACTCCATCAAATACTGGGAAATATGTGTCTCTCATAGAAATGTGATGGAT
CTTTGTAATTCTGATTATCCACAAACCTTGGGGATTAGCTGTTTCAATGT
TCCTATTTTACAGATAAGAAAATGGAGCCTGTGGTAAGTTAAGTGAGTTA
CTCATGGCTACTTAATAATATTTTACTAGGTGATAGGCCAGAGCTAGAG
CCCAGGTCACTTCTTATCAATGCTCTGCCTTGTCTCTGTGCCTTCTGT
CTGTCTGTATGTGTATGTGCTTGTGACAGTAAGGCATAGTTTAAACCCAG
TAGAACTACCGGTTTGTAAATGAATCCACTTGTAAATGACTGACCATTCA
AGGAACAAGTGTTTTTCTATGCTTGACACCTGTTTGGATGCCAAAAAG
GATACAAATGTAACCTCAGACACTCTGGGCCTCATTTTGCACTCATTAGC
ATGTCCAAAATTAAGAAAGACTGACCACCAAATATTGGTGAGGATGTGG
AAGAACGGGAACCTTTCATACACTGCTGGTGGGGATGTAAATGGTACAAT
CCCTTTGGGTAAACAGTTTGACAGTTTCTTAAAAAGTTAGACATATATATT
TACCATATGACTCAGCCCTTCCACTTCTAGGTCTTTACCCAAGAGAAATG
AAATGCTGTGCTTTTACAAATGTCTATACAGGAATGTACATAGCAACCTT
ATTTGTCAATTGCAAAAAACAGAGACAATTCACGTTGTCAAGAGTGAATG

FIG. 4 (18 of 61)

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GATGAGCAAGCTGTGGT...GTCTATGCA...GGTATCCTACTCAGCCAG
AAAGATATGGCTAAT

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GACAACAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAAA
CAAGGATAAAGAAAAATAATCAATTTTGTCCCATTTTCAAAGACAGATAG
CAGCAGCAAGAGTGTAAAGTCTGAGGAAAGTCATATTCCTTCCTCTACAA
CATAGCACACACACTTACAAAAACAATACACAGACTCCTGGCCAATGGAC
TTCAAAACTGAGGAGGATCATTAATTTTAAATGTTTACCCGCTGCATGAAA
TCTCCCTGGGTCTGCCCTCCCTTCCCCACCCTCCTCCACTTGGGCCGGG
GCACAGCAGTGATTCTCTCACCTCTCAGAGTGAGCCAGTGTTGGCTGCAT
TGAAGGCTCCAGATATGCAACAGGGCAGATATTCCTGGACCAGGGTGCA
CAGAGTGAGGCTCCAACGCACCCTATTAAGTGCATGAAGGATGAATGAGC
CTCTGGTATGGGCTGGGACAGAAAAAGGATTCAAGGGGGCCAAAAGGGT
TTGGGTGGAACCTACCAGGAGCGGCAGTACAGACTCCTTGGGAAGGTGGC
CATGATTTAGCCACATTACCAATAGGATAATCTGGAGAATTTCTAGCT
TGAGTTTCTGGGAGAAAGCAGATTTCTGGATTATCTGGTGACAGGTAACA
GGGCCGAGTTTATCCACAGCCACCTGCAGTGTTAGCACCTTAAGCTGAGT
TCCTTGACCCAGGATGCTGTACGCCCCAGTCAGTGAGACGGTTCTTG
CTGAAGGACTGAAAAGCTTGGGTAAGTGACTTCACCTAAGCCTCTATCTC
TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCCTTGCAGGCTTGACTTCA
GGGTAAACAGAGAAAAATGAAGGTACAAGTGCCTTGTGAAGTCTGAAGTCTC
CAAACCAAGTCATTCTCAAAGTGCCGTCCACCAAGTCTAGCACATCAGCATC
ACTGGAAGCTTGTGTTGAAATGTAAATTATCAGGTCTCCAGAGCTATGTA
TGAATTAGAACTCTGGGAATGGGGCCCTGCAATCTATTTCAACAGGTCC
TCCAGGTGATTCTGATGCAAGTTAAAGCCTGAGAACTCTGTCTCTATACA
AATGGATGTCAACTCAAGCTGCTCTTCAGAATCACCTATAGCACTTGTTT
ACCCGAATCCCTGAGAAATGGAGCTTCAGGACTGCTATTTCTCAAAGTTTG
CCTGGTGATCCTGAGATGGGGTTTGGGGGACAGAGATCCAAGGTGCTACC
AGGTGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTCTATAGGGTGCTT
AAAGGTTACAGATCCTAGGATTCTGCCTCTTACAGCTGAATCAGACTTTC
CTAGAATGGGATTGCTGTCCAATGGCATGCCTCCTGGGTGACTCTGATGT
ATAGCCTGGGCTGGGAACCAAGAGGATTATCTTCCATTGACCAAGCTG
ACAACTCGCTTAAGGCTCTGAGTTTCACTTTGATTTTCTAGCCCCTGT
CCTTCCATGGATCACCTGCCCCCTTCCCTCCTAATCAGGAGCACAGTCAG
TGGATGCACTAATGTGGCCTCTCCTTGGCTGCAGGGAACAGGTGGAAATG
TGGCCATAGGTGTGTCAGGGCTGCCCTGCCATGTATTAATAGCTACAGATT
GAAAGATCCAAGGACAAGAGACTAGAAAAAAATTTAAACAGCCAAGCAT
TGGCCCAGTAATGGCATTTCAGAAATCCACCAAAATATTAAGATGCTTTT
TGAAAAATATCCAGAGCACTCATGTAAAGTGCTTAATTATTAATAAAAG
CTGACATGTGTTGGGTACTTCTGTGGGTCTGGCACTAGGCTAATTATGT
TTTTAGGAGTTGACTCAAATGCTCCCTGTCTAATTTATGTGAAAAATAT
AATTATTAGCTCCATGGTACAAATTAAGGAGAGGTTACATAAATAAAAG
GAATGATACTCAAATTAGTAACCAAGAGCCCATGCTCTTAAACACTATGCT
ATTATTTGTGGACTCTTACATAGGTGGCAAAAGTCAAAGGCTAGATTGAC
TTCTGTCCACTTCCAGCCAAGATGAAGTACAAGATTGAGATACACCCTTC
CGCATTAACAACCTTAGGAATCAGACAAAATATACAAAGCATTGTTTGT
ACACATTGGATAACAGACAGCACTAGATAGTCGTGTCTGAGAAAAGCGGT
GAAATGAGCTGAGTCTTAGAATTGCCCCAGTTTACTAAGGGGCATAGTAA
GGGCATAGCTGCAGCACAAAGAAGCAGAACCACAGAGACTGGCGTTCA
CCTGAGTTGAGAAAACCAAGTTGAAAAATTTAGGAACACTAACACAGATAT
GTAGGCAAGAGTATCAGAGAGGAGACAGTTGTAGGGAAAAAGAGAGCTTT
ACAGAGAGACAGCGAGAGCTCCAGAGACCCGCAGAAGATTGCCCTGACGT
CACTAGCTGAGTACCGATCAGTGATACATGTAAGGATATTACTCAATAT
GTGGAAGAAGACAGAAGGAATGATGTCAAAGCTCACCCAAAGACAGGAA
TCATTTATGTTTCCACCAGCCAGAGTGGAACAACCTTGTAAACGCATATGG
AGTACTCAAACGAATATTTCTCAATAATAAGTTCAAATTAAGTGAAGT
AAAGCCTGCCCGCTTTGTCTGGACATGCCTAACAAAGCTTTGAGGGAAGC
CTCAAAAGAATGAAACCGTGTCCAAGTAATTTAACTGTGTCCAGAAAAA
AATTCAAGAACATTTAAATAAATATTTAAATATGATCAAACCCAGCAAGG
TTAAATTCAAAATGTCTGGCATCCATTAAAAAATTACCAGCCTTGAAAAAT

FIG. 4 (19 of 61)

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TGGCGGGGAAATATTA: :ATAATGAA :AAAAAGCAATCAACAGAT
AGGCCTAGAAAGTATACATATGATAAAATTAGCAGACATTAAATGGTTAT
GATTAATTTATTTTATATGTTAAAGAAGGTAGAGAAGAGCATAAGCACAT
TAAAGAGAGACAGGAAAGTCCAGTACTCACACAGGGCCAGGAGCAGTTT
TCACCAAGTCAGGTGGGAAAACCTTCATTTTCATGGAGCATTGGTAGAGTA
CACAGTGTCTTGCCTTAGTAGAGGGATAAATGCTGTTCTGTTCCCGCCTA
ACCCATCTTGAAAGAAAATCTGAAAGGATCAAACCTGTATTCAAGTAACCT
AATCACATCCCAGCACACAGCTCGACTAGTTATAAAAAACAAAAATATTA
ATATCTAGAAACACAAAAATAATATCTAGCACCCAAACAGGTAAAATTCA
CAATGTCTAGCATTCAATTGAAATTTTCTAGGCCATCAAAGAAGCAGTAA
AATATGACCTATAAGGCCGGGCACATTGGCTCATGCCTGTAATCCCAGCA
CTCTGGGAGGCCAAGGTGGGTGGCTCACCCGGAGGTCAGGAGTTCAAGAC
CAGCCTGGTCAACATGGTGAGACCTCATCTCTACTAAAAATATAAAAAATT
AGCCCAGCATGGTGGTGGGCGCCTGTAATCCCAGCTACTCAGGAGGTTGA
GGCAGGAGAATCGCTTGAACCTGGGAGAAGGAGACCGCAGTGAGCCAAGA
TGGCACCAATGCAGCTGCAGCCTCATTAGAGAACATCGGGAAG
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GAAACTAAAGGCTTATTTAAAGCGCGAGACCGTGGCGCCTTTGGACTGGA
CCCTTTCTAATGATCATTTAGTATCAGGCTATGTGGGAGTTGACCGTTTT
GCATAGCCTGAAAGCCAAACAGTATCACTCCTCCTTAGGTGTGGCAGAGA
TGTGAGAGAAGGAGACTGACAGTCTGTGGGTGTGTATGCAGTGTGGGGG
AAGCAGGCACAGGGGACAAATACTGTGGTGTAGAAAACAGTCTAAGGTA
GCATCAGGAAATTCATGAAACC AAAATGAATTTCTAACAGCACAAGACA
TTATTTGTTTTTGCCTCCCTCTCATTTTTTTTTTTTTTTTGAACAGAGTC
TTGCTCTGTCTCATCCATGCTCGTGTGCAGTGGTGCAATCTCGGCTCACTGC
AACCTCCACCTCCAGGGTTCAAGCAATTCATGCCTCAGCCTCCTGAGT
AGCTGATTACAGGTCTGCACCACCCCGCGGCTAGTTTTTGTATTTTTAG
TAGAGATGGGGTTTTGTAATGTTGGCCAGGCTGCCCTGTCATTTTTTTTT
TACTAGTGTCCAGTGGAGTTTTTTAGGGGCTACATAACATGATACTGTCA
TTAATCTAATGGCTAATGAAAGGGATATGTATATGTTTTTGTGTTAAAAA
CAAACCTTCTTTGGGGTCTCAATAATTTTTAAGAGTATAAAGGGTCTG
AGATCAAAGAGTTTGAGTTCTGCTGGACTGGGACAGTGGTTGTCAACCCA
GATTGTACATTAGGGTCTATCTGGGAAGCTTTAAATAGTACTGATGCCCA
ACCTTACCGCAAACCAATTAAGCCAGAATCTCTGTGGATGAGAAGTCTTC
ATTGTCTATCATCACCATGACCATCATCATTGTACCGTCACTACACCATT
ATCATCATCATCATATCATCTTCATTATCATTGTTAGTATCTCCATCACC
ATCATCAGCATCACCATTATTATCATCATCATCATCCCCACCATCATCCT
CATCGGAACCTCACCTGCATGGAGGACAATCCACTATGCATTAGGTGCTA
TGCTATTTGCTATACTCCTTATTCTCACAACCTGCCAGAGAGGCTGATAT
TATCTCACTTTATAACAGGAGGAATCTGGATCGGAAAAGTTAAGGTAAGC
TAATTCACAGAGCGAGAAGAGATAGAGCCAGGATTCGAAACCAGTCTCT
GCTACATCAATGTTCCAGTCTTGCCTTGCCTATTGAGAACCCTCTTTAGTTAT
GCTTTACCCCTCCAACACCACAGTAAATTTTTCTTTTTTTAAAAAAAT
TATACTTTAAGTTATAGGGTATATGTGCATAATGTGCAGGTTTGTACAT
ATGTATACATGTCCATGTTGGTGTGCTGCACTCATTAACTCGTCATTTA
CATTAGGTATATCTTCTAATGCTATCCCTGCGGCTCTCCCCACCCATG
ACAGGCCCTGGTGTGTGATGTTCCCCACCCTGTGTCCAAGTGTCTCATT
GTTCAAGTCCCACCTATGAGTGAGAACATGTGGTGTGTTGGTTTTCTGTCC
TTGTGATAGTTTGTCTCAGAATGATGGTTTCCAGCTTCATCCACGTCCCTA
CAAAGGATATGAACTCATCCTTTTTTATGGCTGCATAGTATCCATGGTG
TATGTGTGCCACATTTTCTTAATCCAGTCTATCATTGCTGGACATTTGGG
TTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCACAGTGAACATTCATG
TGCATGTGTCTTTATAGCAGCATGATTATAATCCTTTGGGTATATACCC
AGTAATGGGATGGCTGGGTCAAATGGTATTTCTAGTTCTAGATCCTTGAG
GAATTGCCACACTGTCTACCACAATGGTTGAATTAGTTTATAGCCCCACC
AACAGTGTAAGCATTCTTATTTCTCCACATCCTCTCCAGCAGCTGTTG
TTCTGTGACTTTTTAGTGATTGCCATTCTAACTGGCACCACAGTAAATTT
TTATAGATTTTATAAGCAAATTGTATTTACTGTGCAAGAATTGGTTTATT
TTTTAAACCATGTGTTGCAAACATACAATGGTTAATTGTGATTTTGCTC
AGTACAAGATCATCAGATCACTACACAGACTTGAGGTAATTCACCTAAA

FIG. 4 (20 of 61)

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AGCAAAGAGAACTGACCCACATTAAGTGAAGAGTCTTTACTTATTTA
CCCTATAAACGAGCCATATGAAGAGAAGGCCTTAATGTGGTTAACTATG
TAATTTTTTTCTGACTTTTTGAAATACTGAGAAGAGCTCATGACTCTCCC
ATCTCCTAATTCTACCTTGGTGGATTTTAGACTGACCACAACTCATGGGT
AAATGAGGGAAGACGAATAAGAAACCTTGCTTTTTTTCTCCTTGTTTT
TGGCTGGCTGCAGTGGCTCACACCTGTAATCTCATCACTTTGGGAGGCCA
AGGTGGGAAGATCACTTGAGCTCAGGATTTCAAACTGGCCTGGGCAACA
TAGTGAGACCCCATCTCTAAAAAAGGCGACGG
GCGGTGCGTGCCTGTAATCCTACCTACTCAAAAAGCCGAGGTGGAAAGAT
CACTTGAGCATGGGAGGTCAAAGCTGCAGTGAACCTTGATTGCACCACTT
CATTCCAGCCTGGGTGACAAAGCAGGACGCTGCCTCAAAAACAAAAAC
AAAACCTTAATTTTTTGCTATTCTTTCTGGTAAGAATGGTATAGAGAT
GGGGATGAGGATGGCTATTGTATGAGAGAGCAAACAGGGTCCAAGCAGTG
CTCTGGGCTGTCTAAGGACCAGTAGTCAGCTTAACTTCTCAAATTTCCAG
GGAAGGAGTTCCGGAGTGGTAGAATATCCTGGGTATGCCAAAGCATCACC
TTGCAAAATAGCCTGTCTGAATAATTTGTTTCATTGTTATGACTGGAAA
CTGGCTTTGTGTATGCCAGAGAATGGGGGCAGGAAAGAGAGATTGGTGTC
TTGAGCTCTCTGTGCCTCTGGGGCAGTGATGCTTTCTCTCATGTGGAA
GGAGAGCATGACTGAAAAGGTGCACAAATAAGGTGTCTGTGAGAGAAAT
AACCTTCCAGATACAGAGACACAACCTTCCCCAAGAGGTCTCATTGCTC
TGCTTTTTCTTTTTTTGCTTGTTCTACCATTAAATAACAGAACTGA
TTATGACCTCAAAAGAGAGGAGAAAGCGACTCTCCCCACCCTAGAGCTAG
TTAACACCATACTCTTCTAGATCTCAGTTCAAGAGTCACTTCCATCCCC
AATAAAAGCCCTTGAGTGCTGAGCACCTCTCGTCAATGCTTGTCTA
GGGTTTTGTACATTTCTTGTTGAACTTGGGTGACATCTGTATTT
CCGACTAGATTACAGTTTCTCAAGGGTAGGGATGTCTTGCTTGCCATTT
TCAGTTCAGCATCTAGACAGTACCTCAAGCAAACAAGGCCGAGGGGGT
GCGGATCAGGAGTTCAGGAGTTCAGAGACCAGCCTGATGAACATGGTGAAA
CCCCGTCTCTACTAAAAATATAAAAAATTAGCCAGGCGTGGTGGCAGGTGC
CTGTAATTCAGCTACTCAGGAGTCTGAGGTAGGAGAATCGCTTGAACCC
GGGAGGTGGAGTTGCAGTGACCTGAGATCCACTGCACTCCAGCTTGGGT
GACAGAGCAAGACTTCGTCTCAAAAAAAGAAAGAGAAA
AGAACATCAAATGAATGAATGAGTGAGATGAATGAGTTAGCAGTGTGGA
TTTAAGTGTCAGATTCTTCCAGCTTGACTTTTTCTTTGGCTTAGTGAT
TTTGAGGTGCAAGATTTATTTCTTTTCAAAAGGTGATCACTACCATA
AGATCTTCAGAAAAAGATGTGGCAAGCCANGTCTCACTAATGCAATCT
CTATAACAACGTATCAGTACT

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GAGGTGTCAATAATATGGACCGATAGATGAATACAGGTAGGATGGGACAC
AATCTAAGATCCCAGGGGGGGGAGACCACACGCTTGGTTAGGGAGACCCA
AAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTAGTGACAGTG
CAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTGCTATTTTAT
CATAGCACTGTGCAGGCCAACCTTCTCTGCTCCACTGGCTGTTGGGAAAA
GCTTTCTTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTTCCTCTCT
CACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGGCTGCTTGTC
TGCTGACTCATCCCTTGGTTTCACTTGAAAAACCTACCACAGCTGGCCT
CTTTCCAAGCATCAGCCTCTCATTTTCTTAATCCCTTAGGTGTGATCTC
ACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATATGAATAAAAA
TGATTATTTTGTCTATCTTCCAATCTTCTTTTAAATATTATTTTATAAT
TCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCTAAGAAATGT
TAAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTAAATGGCTA
GCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAGTGGTGCCT
TTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCATGCTTTCCA
ATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGACCTCTGATAA
CTGCCCCCACCAGTAAAGACTTAGCTGGGAAAGTCAGCTTCATGTGAG
GTAAAAGGAACCAAGTAATACACAATCCCACTGCCAAGTGTGGGTGTG
CAGGCCTGAGCTTCTGTCATGTGGGAGGAAAGAGAAAGAGAGAAACT
CCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCAGAAA
GCTGAATGGCACAGTTACCACTATTGTGCTGAGGTCTGTGGCCTCTGGG
TCTCTTGACAACCTGGGCAAAGACCCACAGAAAACTATCTCTAGACCTAC

FIG. 4 (21 of 61)

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CTGTGGGAGGGGAAAGTCTTCAGATCACTACAGGACAGCCACCTGGAA
CTCAAATGGCTTACAGTTCCCTTCATCCAGAGGGTCTTCATCTAGTACATA
CCAGGTGCTAAGCCTGGGTGCTGGAGACATGACGGGGAACCCATTTACCA
TGGCTTTGTACTGTGACATTACATCTAGGGAAAGCCAGCAAAGGGGAG
GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGCAAGGGAGA
AGCCAGCCTGTTCTGAGCACACACAGTGGTTCATCTAACTGGGCCTCAG
TGCCAGGTGGACTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG
GACACAGATGTCACATAGTCCCTTGAGGTTAGGGTCCCTAGGCATGGCAG
CATTTGCTTTGAGTTTTCCTTTTGTAAATGTTGCCATTATGACAATGTGG
AAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGTTAGGAGAC
TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGGCAGGTG
CAGGGCCCCAGAGAGAAGCAGATGGCTTCCTGAGGTTTTAAGTAGGTAGAA
TCAAGGCAGCTGGTAAAGATCTTTTATTACATATAAACTGGAATAAGCCA
TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG
AATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGAGTCCAACA
CTGGCTGCAATCATAAAAATGTAAAAACAAACAAAATTTGCTAGGTGTGC
TTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGTTATGGCTT
AAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCCCAATGCAA
CAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCTAAGGGTTCT
GCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATTCCCTGATAA
AAGGATGATCTCTGCCCTCCTCCCCACAGCCCTCTTGTGCATGCTTTCTG
CCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCCTCACCAGA
TGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAGAAGTGAAGCCAAAC
AAATTTCTGTTTATTATAAAATTACCCAGTCTCAGGTATTCTGTTCTAGAA
GCACAAAATGGACTAAGATCATTAGATTATCATTTTTTATCAGACTGTTG
AAGTGAAAAATAAAAATCAAAATAAGAAATTAAGAGAGCTGCATGCAGCA
GCTCATGCCTATAATCCCAGCACTTTGGGAGGCCAAGGCAGGTGGATTGC
CTGAGCTCAGGAGTTTCAGACCAGCCTGGGCAACACGGTGAAACCCCTGTT
TCTACTAAAAATACAAAAAACTAGGCCGGGCGCGGTGGCTCACGTCTGTAA
TCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCATGAGGTGAGGAGATC
GAGACCATCTGGCTAACAAAGGTGAAACCCCGTCTCTACTAAAAATACAA
AAAAAATTAGCCGGGCGCGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGG
GAGGCTGAGGCAGGAGAAATGGCGTGAAACCCGGGAAGCGGAGCTTGCACT
GAGCCGAGATTGCGCCACTGCAGTCCGCAGTCCCGCCTGGGGCAGCAGGC
GAGACTCCGTCTCAAAAAAATAAAAAAATAAGCCAGGCATGGTGGTGT
GTGCCTATAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAAATTGCTTGA
ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA
ATCCAGCCTGGGTGACAAAGCAAGACTACATTTCAAAAAAATAAGAAAG
AAAAAGAAAAAAGAAAAAGAAAAAGAAATTAAGAGAAGGGCAGGTATTAA
CCCCAAATATCCCACCATAGGGACACATTAAAGTTTGTCTGGCCACTCCC
CTAGCATATATATGGAATGTCTTCAAGGACCCTCTGTTGTAATAACAAG
GCCCTGCTGGACTTAAATACAACCTGCAGGCTTTGAGATCCCTACTCTGTT
GCCATCTCTCATAGGATTTGCAGACCAATCCAAATACTTAAATAGCAA
CACTCACAACATGCAATCAGAGCAGAAAAGAACTTCTAAAAGGCCCT
GAAACTACACTTTATGAGAGAAGACATAGGGACCTGAGGGTGGTAGAAT
TTTCTCTCTATGCATCTATGTTTCCAGGGCTCACTTTCTCAATAAACTCT
TAAATTGCTTTTAAAGTAAGGGAACAAGCAACATTACATTTAAGAGAAA
TCAATTTTCAAAAGAAGGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT
TGCTTCCATGAATTTGTGTTTAAACAGAAGATGCAGAAAAACACACAATTA
TTGCAAAATCAAGGAAATCCACTCTAAACATCCCTTGGTTTCCCAGGCCA
GTGTCACAACTGAAAAACATATTGTGGCTAATTATGTGTCACAAATTAG
AATGACAAGGCAAGAAAAAATACTCTCTGATTAACTAATAGCAGCCAA
CACAGACAGCCTGTGTAGCTCGACTCTGCTGGTTTATAAAGGCAGAGA
AGCAAAACGGCTTCTGTGACCGCAACAGGAAGGGCCTCTGCTCTTAATAAA
TAAATAACATTTAAATTATTCTCCCCCATTTGCAAGCATTTCCTCAACTC
ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTTGTATAC
NAAATAAAGAATAAAAAATAAATATGGGCCANGCACAGTGGCTCATGCTT
GTAATCCCANCACTTTGGGAGGCCAGGCGGGTGGATCACTTGAGGTCAG
TAGTTTGAGACCAGTCTGGCCGACATGGCGAAACCCCGTCTCTACTAAAA
ATACAAAAATTAGCCCCGCATGGTGGCAGATGCCTGTAATCCCAACTACT

FIG. 4 (22 of 61)

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TGGGAGGCTGAGGCACGAGAAATTGCTTGAAGCTCGAGAGGCGGAGGTTGCA
GTGAGCCGAGACTGCGGCCATTGCCCTCCAGCCTGGGCGATGAGAGCGAA
ACTTCATCGAAAAACAAAAACAAAAACAAAAACACCTTAGAAGA
AGCGTTCTCTCTCTGCTTTCTGAAGACACTCTACGCTGAAACAGTAACT
TTCAATAAACCATCTCTCTCACCGCACTCTGCGACTTGCCCTGAATTCC
TTTGTGTGCAAGATCCAATAAGCCTCTCTTGCGGTCTGGATGAGAACCCT
TTTGTGGAATACTCTGACACAACAAATTGCAGAAAGAAAGTCTCACATG
TATAAAATAAGCAAAAAGATTCTCTGGCATCTGAAGAAACAAATTCCTTG
TCAATATTAGTATCACTATAAGTGTAGAACAACCTGTTGTATGATGCTAC
ATAAAGTATATGAATCTGAATACTGTTGGATACAAAGGGAGACTATNNAA
TGTAATACGTCGCCCCGAAATGACTACACTGTTGGTGATCTTTCTTTCAAG
AAGCANAATATTGCCTCNAACATCCTGTACATGGTATAAAATTTTA
>Cont1g44
CCCAGCAAGAACACCAATACAACGGGGGGGGCGTTCTTTGTGAGGGGTGG
GGAGGTCAATTTTTTGGAACTGCAGCAGGTAACACACAAAACCTTCACA
GCTGCTACCAGCTTTCCAGGAGAGCCTGTGTACCTGGAGAGGGAAGGCA
AGTGCTTCCGAAGCTTGACTTGATGTCTTAGATTCTGCAATGCGTAGTCTG
TAGGGACAGGCTGTAGCTTATCCTATAGGCTTGGGCTGGAGTCAGCAAGC
ATCTGGGCTGGCAGAAGATAAAAGATGCAAAGGTGGAGGAAAGCATACGT
GGTCTGGAAGACAGACTTGGTGGGTGGGTGGCTGCTACAACACCCTAGTT
AGAGGTAGAGGGGTAAAGTCAGTGTGTCTTCTGCACAGGCCTCTTCCCCAC
CTCATTCTTCATTTCCCATACAGCCTTGCTGAGTTATTACAAAACATCTG
ATTCAACTGGAAGCTGGGTTGAGGATGACCTAAAGGACTAGTGTGATGCC
TGCCCCAGGGGTGTGGGCCCATAGTCAGAGTCCAGAGCCTCCTCTCAGCTT
TTAGCACATCTCACCCACATCCTGGGTCTTAATTAGCAATATGAAAGCA
AGCCAAGTGACAAGATTTTGTCCCTGGGAAGTCCAGAAGCACTCCTTTTC
TCATTTGTATAAGCATAATGATTTGCTTACATAAATAATCATGAAAATTC
AAATCCCTCTCAGAAATCAGGTCAATAAACCATGAAATGCAGCATGTGGG
CAAGAATCACAGGGAAGGTAGGTCTTGAAAAGAAAGGATGGCAGGGAG
GAAGAAAGCAGGGTGCCAGGGGCCCTGGGCTGCTGTCCAAGTCAGGTGGC
TCACCGTCTCTGAGAACATTTCACTTTCTGGTAAATGGGGCAGTTGGAGA
TAGAAGGGTTGGGTGAATGCCAAGAGTGAGCACAGCTGAGGTCAGTGCTG
TGCCTGCAGTCCAGGCGGGAGTAGAAATCCTGGGCCCATCTTACCTCCGA
CCTCATTCTCTCTCTGTAATAATGTGGGGGTGGGGGAAAGTTCTGGTCA
TCAGCCCTAGCATTCCATGGTTCAATTCCTCATCAGTGATGGAAAATCAC
CAAGCAAGAGAACAGGATGGAGAATAACCGATGGGTGCAATCGGAGGTG
CTATTTTCAGGTGAGGTGGCCAGGGAAGGCCCTCTGAAAGGGTGGCTTGAG
CAGGTGGCTGAATGTACAGAAGCTGCCAATCATGAAAGATCTGGGGTACA
GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCGAGATTGGATGTG
GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC
ATGAACAATGGGTGGAGGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCCA
GGCTTGGGTAGGAGAGGTGTCAACTTGATATATGATGCAAAGCCCTTGGA
GGTTCCCAACACAAAAGCAATGATCTAATATATGGTTTTAAAAATGCCA
CTCTTGGCCCGGGCGCGGTGGCTCACGCCTGTAATCCAGCACTTTGGGAG
GCCGAGGCGGGTGGATCATGAGGTGAGGAGATCGAGACCATCCTGGCTAA
CAAGGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAGCCGGGCGCG
GTGGCGGGCGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAAT
GGCGTGAACCCGGGAGGCGGAGCTTGCAAGTGAGCCGAGATTGCGCCACTG
CAGTCCGCAGTCCGGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAAA
AAAAAAGAGTGAATGTCAAAGTGAAGCAGACCACTCAGGAGGTGAGG
GCAATGGACTGTGCAGGAGAGACTGACATCTTAGACTCGGGCAATAGGAG
AGAAGGTGGTGAGGATTATATTCTGGGCATAAAGGCAACAGAACTAGCTG
ATGGCGTCAACGTAGGAGATGAGGGAAGAAAGAAATCAAAGGGCATTCA
TAGGTTTGGAGGTTGAGTAACTGGGGATATTTAACAGAAATGGAGAAGTC
TGGGGAAGGGGCAAGTATTGTGGGGCAGGGGTCAAAGTTCTGTATTTT
GGCCAAGTTAATTAATATTGAGATACCTCTTAGGTGTCCAAGTGAAGAT
GTCAAACAGTCAATTGAATACAAAATCTGAATCTTAGCCCAGGATGGTCT
CACACCTGTAATCCAGCACTTTGGGAGGCTGAGGTGAGAGGATCACTTG
AGGCCAGGAGTTTGTGATCAGCCTGGGCAATAGAGCAAGACCCTGTCTCC

FIG. 4 (23 of 61)

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ACACACACACACACACA. AAAAAGTCATCCAGGCATGGTGGCACATGC...
GTAGTCCCAGCTACTCAGGAAGCTGAGGCAGGAGGATCACTTGAGCCCAT
GGTTCAAGGCTGCAGTGAGCTATAATCACATCACTCAATACTACACTCCA
GCCTGGATGACAGAGAGAGACCTCATTATTATAAAATAAAATTTAAAAAAA
TTAATTAAAAATAAATCCAAATCTTCTGAGATTCAATTTCAGGAGTAA
CTGTTCATGTAGAAGGCATATAATGCCATGGGTACATGATACCATCTAAT
GAATGCCACTGGAAAAGAGAGAATAGCTAAAAACTGAGCACTGGGCACAC
CAGCACAGTGAGGTTTGAAGGAAGAAATGGAGCTAACAAAGGAGACAAAA
GAGGAGTAGCCAGTGAGAAGAGAGAAACATCTGGAGAGAAGAGAGAGCAG
CAAAAGGTGGGTGAAGGAGAATGTGGTCCACCAGGCCCAACAATGCTGAG
CAGTTGAGTAAGTGAGGACCTGGCCACTGAATTTGGCAAGAAAGAGGATG
TCAGCGGCCCTAGAACCAAAAGTGAAGAAGAGCTTGAGGACGGAAGCCTGA
CAGGAGTGAACCTGAGGAGAGAATGAAAGGTGGAGACATGGAGCCAAGGAG
CACTGAGACTCCCTTGAGTAGTTTTGCTGTAAAAATAAAAGTGAGTGCGA
GACGGGGCAGGGGGACAGAGAAATGCAGGGGTAGCTGGAGGGAGCCACAG
AATCAAAAGAGGGTTTTTGTGTTTAAGATGGTAGTTGTACATAGCACAT
TAGTAAGTTCATGTGAATCACAACGTAGGTGAGACAGATCACTAATGCAG
GAGTCAAATCCTTGACAGAGCCCCCAGAGGAGGTGATGAAGGGAAGTGATG
GACATCATTTCAGATGCAAGTAGGTTAGCAATTCCTGGGTACAAATAGGA
GGTGACTCCTTCTGATTGCTCCTGTTTTCTGAATGAGATAGCACATAAA
GTCCACTCAGCCATGTTAGCTGTTGAAGTCCTTGTGGCTGTCTGCTGT
ACAGACTGGGCTCTCCTCTCCAGCATTCTCCTCTCAGACTAAGCTGAGCTG
CACTAGCCGCTGCCACATCCTCTTGGGGCCATCCTCTGCCCACTCCACA
TATTGCTGTGGTTTGTCTTGAACCCCTGGAAGGTCTACTGGCTGCTCCT
AGAAGAGTCTGGGCGGCATCTCTCCCTTACTCGTTATCACATGGTGCTGT
AAGCAGTGGCCACACACTTTAGCTGGTGGGATGGGCCATCACAGGCAGTA
AATGCCGAAAGACTGCTCAGATTTTAAAGCACCATGAATCAGTAGAATGA
GTTTAGAATTGTAGTCATCAACACACATTAAAAAAGGATTTAACTACAAC
CCAGATAGGAGGTGCAAAATTGTCTTACATAAATCAGATGGAAAAAGTT
GAAAGCAGATAAGATAAAATAGGTAAGCATGACATTTAAAAGGTATTCAT
GGGACGTGGTTACAAAACCAACTCACAATAAAAGTCTTAGGACCTCTC
GCTGACTTAGGAGCCTGATCCCACTTTGAGAATGACTCAGTGTTTACC
CTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGAGTCACTAGCCAACAG
CCCATATCAAGTAATTGAACTTTGACTCAGAAACCTCAGTGTGAGAACC
TTTGACTTAGGAACCACCTGTAGTGGTTAACTGCAATTTGCACCCCTTAG
TTCAGGGCTTTACAACACCGGGGGGGGGGAGGGGGAAGGCATAGAGCTGA
TGACCTAAAGGAAACCCATTGCAGCAACGCTTTTGTGTTAAGTTTACAAA
TAAGTGTGTTTTTAGAATCCTCCAGGTAATGCCTTTGTTATTTAATGTGT
CTGAGACAATTCTGCACATTAAAGAATATAAAATATTACCTTGTAATTCC
AATTTGAAATGTGTAATTGACATTAGACTTCTATTTAATTTGAAATGTC
TAAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTGAATTTTGAGTCTGAT
TTACTACATTTTTTTTTTAATTTCTTTTTTTTGGAGTTTAGGGATTGC
TTAGATGGCTAGAAAGATCGCTAGGCACATGTCC

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GATGTGTGTACGTGTGTGCAAAATACCGTGCCTTTTTGTGTTTTCTTTTGT
GAAACAGAGTCTCACTCTGTGCGCCAGGCTAGAATGTAGTGGCGTGATGT
CAGCTCACTGCAACCTCCGCCTCCAGGTTCCAGTGATTCTCCCGCCTCA
GCCTCCCAAGTAACTGGGATTACAGGCGCCCAACACGCCCAGCTAAT
TTTTGTATTTTTAGTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTC
TCTAACTCCTGACCTCGAGATCCACCCACCTCGACCTCCCAAAGTGCTGG
GATTACAGGCATGAGCCACCATGCCTGGCCAATACTGTGCCATTTTATTA
TCAGGACTTGAGCATCCATGGATTTTGGCATCCATAGGGGTCTGTAAAC
CAATACTGCACAAATACCAAGGGACAACCTGTATTCTAAAAAGACCAAAAA
TTAATAAGCAGGACGCTGAAGGTAATTGCCCAATAAAGTCATGATCCCT
TGCCCAAGTGTCTGAACCTCAGCCAGTTTTCATACTCAGGACCTATTGGCT
GCAGAGGTGGTAGGAACCATATGAGAATCTGCAATATCATGGCAAGTAT
GCACCTTAATGATATCTGCAGTCTTCCCCAAAGGACCTTACATTTACC
ATACTGCTATGTCCTGCGTGAGAGGGTAATACTCAGATTTTTTTTTTTTT
TTTTTTTACACAACGCTCTTACTGTGTGGCCCACTGGAGTGCATGGCT

FIG. 4 (24 of 61)

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FIG. 4 (25 of 61)

GAATGTGATTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTACT
TTTATTTTAAAGACATAGAAAATAAAGTAAAGATCAGATTGCTTGGCT
GGGCACAGTGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTG
AGTGGATTGCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTG
AAATCCCATCTCTACCAAAAATACAAAAAACAACCAAAA
AGAATAAATTAGCTAGGTGTGATGGTGCCTGCTTGTAGTTCCAGCTACTT
GGGAGGATGAGGTGGAAGAATTGCTTGAGCCAGGAGGTGGAGGTTTCAG
TGAGCTGGGGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACT
CCGTCTCAAAAAAATAAATCAGATTGCTTTATTGCTGGTTTTCTTTCT
AAAACCTGAGATTGGGTCCCATCATCCCCTGGCCCCCATTTGGTTAATGGTT
CCTCCTTTTGTCTATTGAAATAAAAATACAGATGTCTGCTTTTGCAACATGG
TTGAATGTAGACACTGCAGGGTCTTCTGACTCAAAATGATTAGGCTTA
GATAAAACACATTTGGAAATGCATTTCTGGATTAAACCAAGGAAAGGAG
ATCTCTTTAAATCCCTTTCTGTTCCCCCTCCCTACCCCTCCAATTGG
GCTTAAGTAAGAGGGTGGTTACCCGCTAGTAAACCCCTTCGAAGGGGG
TCTTCTCTCTAAGGGAAAACCCTTGTTTTGACATTTGCTTCAATGGGCC
CTTGATTTTGTTCCTTGCTAAACGGGTGCTAAACCAGGGGCTCCTCTT

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AAGGCTTTTAGAATATTTGCACACTTTAGAAATGGAAATGTTTTTGGGGG
GCGAGTTGTCTTAATATTTTCTAGCTTGTGTGACATCCTTTTGA
AAGCAGCAATTTCTGGCCTTTGTGAGAGATGGTGAATGCCTGCAGGTGTGT
GGACCAGTGCCTCCCTTCTTCTACATGCACGGCCCCCAGCTGGGCCCCA
GCAGAGTGTCTGTACAGAATAATTTCCAAGGGCTGTGTCTTAACCTTTG
GTCTTGTCCCCCATTTGCTGTAGATTGGCCAAATTGACTTCATAAGTGCCT
CTTATGAACATAGATGTTGGCAATGGAAGTTGAGGACCAGTCAGTGTTG
TTTTATTGAACACACAGCGTAAATCCCAACACAATGCTGACCTAAGAGAA
TTCCAGCCACTCTGATTCTCAGTCTCTTTATATCTGAAAGGGTTCTGTTT
CACTTTTCCCAGATCAAAATGTCCCTGCAGCTACTCAGCAGAGCTGTCTG
CAACTTATACGTAGAAGAGGTAACAGTCCACAAACAGAAAGGCACAGGAC
GAGAGTGGTCTGGGTGATGCTTCTGTGGGGGAAAAGGTGATGAGGGTGC
ATCTGCACACCTTATGTTTATAGGTAAGTCTGGGAGGAGGTGACCTCCCT
TTGGTTGAGGTGCTGAGGCGTCTTGTTAGAATGGCACTATTCCATTTATC
TGATGCAGTCTGTGGGAATTTTGTGGTATGGCCACCACAGGTACCATGCT
GGGAACCAATGCCAGATACTGCCTGCTAAGCCACAGCATGAGTCACATGAG
CATTTGTGGGCTTTGGGAACTAAAGTTATTGAACGATAGTTATCTGAAAA
GGAATTTAGGGAAAGGGGACTTTAGTCCAGCGAACAGTTTGCAAAACCAGG
GGGAAGGCAGCCTTTCAGCGTAAATGAAGACGTGTGTGCCCAATAACA
AAGGGAGAGTTTGTCTTTTAGAGAGTAAATGTCCACGCAAGGTTCCACTT
AGGCAATGAAAGATGCAAACTTGCTTAGTTCTGATTGTTTACATTTGC
TGAATTCGGATTGGTCCGTGCAGGCTTTTCTGGGAACTCCAAATACATGT
ATGACCTCTAGTCATACATGGCAAATGGCCGCTTGGCTCTAATTTGAATT
TAGGCCCAGTTAGTCACTCAGGATTAACCTTTTTCAGGGTTCACAGCTCT
GAACAATGGACTTAGACCTGCAGGACATAATCTGTTCTTAACCTCTGGGAC
TACCTGTGCCTTTTGAAGTGTGCCCAGTGAGCAGCTGTGGCTCTGGGCCCA
GACCCACAGGGCGATAAGGCCACAGAGGTACGATGGAGCAGGCTGTCTCT
GCTGAGTGATCATGAAGATACACTTACATAGAGCAGCACTTTTCTTCCA
GTCTTTGTGATTTAACTCATTAGATCCTTATAACAAGAGTCAGTCTCTTA
TTTAACCCATGAAGCACAGGTGGAGTCCAAGCTTAGTTTGTGAAGGATGA
GCCAAAAGGATTCTTCTCTGTAGACCTCAAGCTCAGCTCTCTCCATGGG
CCCTGGAGTAGGTGAGAAGGCCTCTGTCTTCCAGAGCCCACTGCCAATCA
TCTACATTTTCTGTTAGCCCAATTTAGGACATTTGCTTTACCACTGAAG
GGTGAGAACTATCATAAGTTATAAAAATCAATTGAAAAACAAGGTAC
AGAACAGAAAAATAAAGATGAGAATCTATTAAACATAGTGATGTTACTGG
AAAAGGGGGTCTCAAACCAGACCCCAAGAGAGAGTCTTGGATTTACAC
AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGGTGAATTGAGAGAGTTTA
TTGAAAGCTATTCCATTACAAAGTAGAGCATCTCAGACAGCAAGTGAG
GAACATGCCATCATTAAATTTTCTTATATAGGAATCTTGTCTATATAAA
GACTAAACTAAGCTGTGGCTATGTGTGGGTGGGCCGACAGCATGAAAACA
TTTATTCTCCTATTGATTTAAAGAGAACTATCCTTGACATTTTAGTGTGT

FIG. 4 (26 of 61)

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TTAAGTACATCAAAGCA1AACTATAATTAAGCTTGAAAGCATATATTTTAA
TAGGGATTGGGACATCTGGGCTTTCTGTTGTTGTAGAAGTTTGTCTTGC
AGGGATTACCAAGCCACTTCTTAGCTGTAAACATCTTAGGGCCATGGGT
CCTGACTGGCAAGGAATGTGTCTTGCTAGTTTTTAAGATGGGCTTGATTG
AAAATGGTGTCCATCTGGCTCTCCTAGGCTCCTGCTTCTTAACAGTAAG
GGTAAATGCTATGTTATGAAATGTCAATTTCTGCCTTTAGCTTGCAAACCTC
TTGATGGTGAAATTCTCCTGTCCGTTTTTCAGTGGGGTATTTATTCTGCAT
CCACGTCTTCAACAAGGAGCTGAAAACAAATTGGATGGAAGCAACTGGGT
TTATGGGACACGTTAATGTTTTAATGTCAATTTGGTGTGGAATTCAGATGT
CCAAGCAACATTTTACACTACAAATCTGCAACTTTAATAATCACTCAAAG
TACCTGAACCTCAATGCTTTTACAGACAGACTTGGTATAAAGCCACCACCTC
TTTCTATTATGGCAGCCCTATCCTGAGGACACAAATTTCTGCAGGGCTTC
TGGCATATCTCTGATTAAACAAATGTCAACAAGGTTAAACAAATGTCAT
CTCTGATTTGTTTGTGTTTTAAAGCCTGGATTTACTCATTGAATATTTCACT
CCTACTAGCATGTCTTGTAGTAGTTTTCTTCAGGGACCCTAATTATTGCT
ATTAAAAATATGTGTGCAGCTACATGTTTTTTTTTTTATCAATTTGCAATG
AAAACCTTTAATGAATAATCTATTAGTGTATTATTTGAAAGTGAAATCT
TTTCCTTTTGTCTTTCTTGTCTCACACATAGTGCAGACAGTTTCCACAG
GGCTCATAAAAGGAATGATTCTGCCTTGTGTGAACCTTTTGCCTTTATTG
TTAATTGCACCATTTTGTGACTGGCTCTTGACCCTGTTGTAACCAAGCT
CATAATGTACATTATTTCTATTTTGTCAGTTGTAGACACTTGAGGAAGTT
CCCATTCTTTGTTTCTTCTTGTCTTTGTTCCCTGTGATAACTTTTTCATG
CAGACATTTTTTTTTTTTTTTTTTTTGGAGACCGAGTCTTGCTCTGTCTATC
CAGGCTGGAGTGCAGTGGCATGATCTTGGCTCACTGCAACCTCTGCCTCC
CAGGTTCAAGAGATTCTCCTGCTTCAGCCTTTCTAGTAGCTAGGATTGCA
GGCGTGCACCTACCACACCCAGCTAAATTTTTCAAATTAGCCACCCACCT
GGCTAATTTTTGTATTTTTTAGTAGAGACAGGGTTTCAACCATGTTGGCCA
GGCTGGTCTCGACCAGGTGATCCACCCGCCTTAGCCTCGCATAGTTGCAG
GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCCAAGATGCGGT
TCCAACATGTGGCCATTCAATGTCTAGGCGCCCTCTACTGGTCTTGGGAA
GCGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG
TTCTACAGGTGACCAAGGGCAATCTCTGGAATCCTTAGCCGCTAGGTCC
TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGGCTGAGGATGGCTCTCTTA
GACATTTGTGATGAACCAAACGTGTGCATTCTGAAACTTCTGTGAGCAA
GCAGGTGAGTAGAGTTGGGTTATAAAAAAGTCTTAGGGTCTCACTACAGAG
ATGGACTTGTCTGTGTAGATGGTGCAGAGCCGCTGAAGAGTTCTACTTGGG
GTAATGGTGTGATTGGGTTTGCCTTTTAGGAAGATTCTTGGCCAGAATG
AGGCGGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGCAGTTATG
GGCCACTAATCCAGGTGATAAATGGTGTCTCTGAACCTCAGGTGGGGGTG
CCACATGTCTCCATCTGCTCTGTACCCTTGAGACTGGCCTTATGGGCTGC
CTTAGTGGTCTGTTGTCTCTATCTCCTGGTTGGGCTCAGGCAATGGGAG
ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGCACCCGCGCCCTTTCAG
GTTGGCAGTGGCCACATTCCCCTATACAGAAGGCCACAGTTTCTGTCACT
GGCCCTCCACAGCCCCAGCTTTCTCAGTGGGCCAGCCACCTCCCCATCC
CTTGCTCCTCCTCCTCCAGAGAGGGTTGTGGATTTCCTGTCTCAGCAGTG
CCTGGAGCTCCACCATCTCCTGCTGCTTCTCTGGACCTGCCTGCAGTTT
TATAAATAACCTTTCTTACATTACCTCTAGCATGCACCTTTTGTGTGTA
TACTCTGCCCCCTGTGAGCATGACTCATGCCAAAGAGTTTGAATTTTT
TTCTCCAGGCAACGGGAGGTCAATTGGAGGATTTTAGACATTGAGAACAGA
TGTTGATTGTGGAATATCTGTCTGACTGAAGTGACCAGGATGGTCCAAA
AGAGCGAGAATTTGAGGCAAGCAAACCATCAGCAGGCCAGCAGCAAAAT
CCAGGTCTATAAAGGGAAGCTGAGGCTCACAGGGTTGGATCAGGGAATG
GGAGAGGGAAGCCAAACAATTCCATGAGCATGTGAGTTGCACATATGACT
TGGTAATATTTTTATTTTTATTTTTATGTTTGGAGACAGAGTCTCGCTC
TGTACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTCTGCAACCTC
TGCCTCCTAGGTTCAAACAATTCTCCTGCCTCAACCTTCCAGGTAGCTGG
GACTACAGGTGCGCACCCTACACCCAACTAAGTTGTGTATTTTAGTAG
AGATGAGCATTACGCTGTTGCCTTAGACACGG

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AATATTGATTATTTGACCAGAAATTCATGCAGCTAACCGTGACCCCTGGC

FIG. 4 (27 of 61)

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AAAATAAAATAGTGTAT...GTACGTGCAATATACATGCAAAGAAATGAG...
GAAACTAGAAGGATGTCAATCAAATGATAACATGGTCATCTTGGGGTCGG
AGTACATTTGGGGATGAGGGAGCTGTAAAAGCAGACTTGGACCTTTTCT
TCTACCAGTACCGTGTCAATTTGAATTTTGGAAAGAAAAAAACTCAG
AAGGAGGAGAAGGAGCAGGAGGAGAAGAAGATGGATCTTAAGTGATTTC
CCGGGAGCACCTTGAGAAGGTGAGATTCAAGTCTAGGTCTAAGCTTTCTA
ATCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAAGGAAGA
TGTTCTCCATCATCTCTTGCTCATCCTAACAGCATGCAAACCACATCCA
ATGCAGCTCAGAAAACCTCCCAAATTGCCAAATTTCAATGGAAACACTTAA
TGCTGTGGTTTCCAAATTTCAACTGTAAAGTAGGTATGTATGCCATTGTTA
CCATTAACCTTCTCAGAAATGGAGAGAGCTCTCTTCCGCCTCCTCCCCCT
CTGCTGTGGCTTTGGTGAGACGTGCACTCAGGCTCACCTGTCTCCATGAT
CTCCAGTAAGTACACATGAGCAGAGAGGCCTCAGCTCAGCTCTTCTGGT
CCCACCAGGGTTGATTCTTTGAGAATTTAGAAATGCCACATCCTAGGCCC
CCCAAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAATT
TCAAATCAACCATCGTTTAATACTCACAGACTGGGCACATCCAAAAACAT
ATTTTCAGTTTTTACAACAGTGCCTGGTGCATATCGGCACTATTTGTGGAA
GCAATAAATCGACACGGAGCTGAAACACAAACAAATGCCAAATGTTTTT
ATAACACCTGATTTTCTTTCTGTTTCTTTATGCAGTTTAGTTTTGTTTG
CTTAACCTCTACCTCAGACCATAGTCTGGTAAACTCACCACCCAGAAGCTC
CCTTGAAATGTGGGTATGCAGCCACTAGGTGGCAGGAGAGAGTTTTCTGC
CTGGAGGGAGGACAGCCACTCTGTCCCCGGGTGAGGCCAGGGCCACCCTG
CTACCTGCAAAATTAAGCATGGGGCTTTATGAACACAGCTTCCTAATAAA
CACAGGATCTGTTTGATAGAGACTCCAAAACACGCCTACCTAGTGATGAA
AGACTCAACTTCAGAAGAAAACCTTCATGGCAAACATCTTCAGAGATGTT
TCCAACCTTAAGGTTCTGAACACAGACGCTTCCCCAGAAAGCCATTGTTTC
TCAGCACCTGGGAGCCTTGCTTTGCTTTGCTTACAGACTCGCTGTTCTTA
AATCACTGCCAAGATAACATCTGTCTCTTCTTACCTCTATTTTCGATA
TAAGGACTCCTCACTCTTGTTGCTTCTATTGGCTACCTCTCCACAGGGA
GAAATCGCTGATTTAACAGCAGTCAATATCCCAAATCTGGAACAGGGAAC
AGGGAAGCATTTAAAAATTGGAGAATTTAGGCCGGGCAAGTGCTCATG
CCTGTAATCTCAGCACTTTGGGAGGTGACGTGGATGGATCACTTAGGAG
TTCGAGACCAAGCCTGGGCAACATGGCGAAACCTCATCTCTACAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAACCCAAATTAGCCGGGCATGGTA
GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG
CTTGAGCCCTGAGGTGAGGCTGCAGTGAGCCGAGATCACACCACTGCAC
TTCAGCCTGGGCAACAGAGTGAGACCTTGTCAGATAAAATAAATTAAT
TAATTTAATTAGAGGATTTAAGGATTTTCCCTACAGACACCTCCTTATTT
TCTCTGGCCTTTTCTGACTACTCTCCCTAACTCCCTGCTCCTCTGGTCTC
CCAAAACCTACTCCAGAAAAAAAAGGGGGGAGGGACTAAAGGAAAGCC
AGGTGACAGTGCCAGTGTGACAGATGACAAAGCATCTGCCCGAACAAACC
GTAGGTCCCTGAACTTTCTCCAAGACCTGTCTGTGGACTTACCTATGAAA
ACCAGTTTTAGCAAAAACCTCCTAAGCCAGTTTATCAAGATCCCCTTAT
CCTCAATATCCATCTGATTGGATTCTTCATCCCCCACCATTCCCCAGTGA
TGTCACCAGGCCTTTCTTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC
GCCCCCTCACCCCTGATATGCCCTTTTAGTAATTCTTCATCCACAGGTTT
CCACCTGTCTCCTAGGCTATACATTCCCATTTGCCCATGCTGCATTCCGA
ATTGAGCCCAGTTCTATACTGAGGTCTTACTTCACCTCTCGCCATAGTCC
TGAATAAAATTGGTTTTTACATTTAAAAACTGTCCAGCTCTGGTTGTTCC
TTGACACAGGGTAATTTTTATTCCATGTGATAGTTTGCCTTACCTCAGCC
TACCCCCCTCAAACCTGCAACTCTATATTCAAGAACCAGACAGCCCTTTC
CAACAGATAGGAAGAGGCTGCCCTGGTGCAAAGGAAGAGGCTCTGGGAGG
AAGGAGAGAACCCGAAGGCTGCCCCCTCCTCTAGACTGAGCTCTGGGATG
GGTGGACGATAAAACCCAGATACGTTTAGACATCTGAGCGTGGAGAGGAC
TTTGCTTTGCTTCCACAGGGACCCCAAGGAACTGCAAGCCCTCCAGAGA
CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGCAGAATC
ATCCTATGTGGGCACAGACACAAACAGAGTCCCCTGTGGCCCCAGGAGAG
TTTAAAGAAGATCCAGAGGCTGTCTTATTCCATATCTCAGCAGAGACAGG
CCCSTGAGCCTAAAAGCTGATCATTAGGACAAGAAGGACACGAACTGTCC
TGCAGCGTGAACCGCTGGAACAAGGCCAATCACCAGACACCAGACCAGC

FIG. 4 (28 of 61)

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CAGACACAGCCCCGCGAGTSCCCCAAGACACCACGGACCCATCGCCCCCTC
ACCAATAGCTCCAGGCTACATAGACCCCCCTCCACTTCATGGATGTCCTCA
GAGCAGAAAGGGGAGGCAGGAGTGGAACCCCTGACTTGGTTCAGTTGAAAC
ATAAAATGACTGTACTATTATTGAATTGCTGAAGTTTACGTGAAAGAAAT
GAGATTTAGTTTTTGGCCACAGTGCAAAATAAGAAACGAGGCTTCAACTG
AGATTAAGGTGAGTTATAGGAAAATGTACTCCCTTGAAGGACCTGTGAAG
TGTTGTTGCTATGAGAAAATGACCAGAAATCCACGTTCTTAGCTGCGGGAC
TCAGGCTGACTCCTGTTTCTGGAGCTTGACAAAAGGGCAGGGAAATCCCT
GTTTCAGGCACAGTGATTTCAATGTTTAAAAGAAAACAGGTGGGCCCTGG
CAATCATGATAACATGTCATAAGTTTACATCTCTGTGAGGCAGGTAGTGT
AATCCCCATTTTGCAAAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT
CTCTTCAATGTGGCCCAAATGTTGGAGAACAGAGCTTAACTGAATCAGCA
ATTCTATACTTAGAACTGACTCTCTCTTTATTATATCTCACTACTACCTT
GATATTTGAAATATTCAACTTTTTTCAATCAAAAAATAACAATAATTTAG
GCATAATGACTACTATGTCATTTAATTTCTTGCTGATATTTCAATATCCC
ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA
ACTCCCAACAACCATCCTTCCAGAAATATTTTCCCCCTTCTTTTGTATA
GAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTGAAC
ACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAAAACACATACC
AAATTTCAAAGACATGGCACATAATAAAAAATGTAAAATATCTCATTAA
AATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTAAAT
ACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACTTCA
CATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCTATT
AATGTCGTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAATGACATA
TAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTGCTG
CATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACCTATCAGTGACATTTA
GTGAGGACTTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTACTTA
ATTCTCTAAGCCTGGTTTATATCCCTGCAAAGAGAGAAGGATAATAATC
ACCACTACTTAGTGATGTCGTAAGGAGAAAATAAAATAATAAATATGAAA
TGGCTGACAGTGTCTTGTGTCACACAGAAGATGTGTGATCCACAGTAGCTG
CTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAATGT
GCATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGACCAG
GCTCATCTAAACACAATAGGATGCTTGTGGTGTTTTGAGGAGGAATCAAG
GACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGGCAC
ACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAGCTG
TGGGTGGTGGTGAGTCAGACCCAGCTTCCCTCTGTGCCTGGCTGAGTGGT
TCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCCATCTATAGAGA
GGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCCTTATTTCTGCTACT
TTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCCATT
TCCTAATGTTCAAACCTAGCCCCAGAAACATCTAAATGAATCAAACAAAT
AAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGCAAC
ACACACACACACACAGAACCCATAAGCCTTCATCTTCTTGGATAAA
CGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTCCA
ACTCGCCTTTTGACAGCTTCAGATGGGTCTTCTGCGTGGCAGTGGCC
CTCCTGACTTATGATTTCTGTGTGTGCGCCTGTTACCACTGCAGCTTAA
CTGAGGAAACAAGAACAACACAGCTTCTGACCCCAAGAGACTGTTGGAGG
CAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCCAG
CCCTGACCTTTTCTCCAGTAATAACATAAGAAAACAACAGGCCTTGGCCTT
ATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTCAGG
GCTACCCCTTCATGGACGCCCAACATCCATGGTTCCTGCTTGAGTCCCT
GCTTCCATATCTGCACTTCTCACTTGAAATATCCCTGGAGTACGTTAA
GCAGCCAGGTTTGAAGTTCTTGTGTGTCAGGCGGGTGTGTGATGTCCT
CTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCACGC
CCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGGGGC
CCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTATGCGCC
CTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTCTCT
CCTGGACAATCAACATGAACCTCTCACCCTCTTATCCACTTTGCATAAA
CTGAAAATAACAAACCCAGGGCTCTTTCTGTACAGGAAAGGGTTTTTTT
TTATAAAATTAACAGAGATGATTCAACACACCCAGGATATAACACATGG
GCCATGAATCAAGGGCAGCATTGCTCTGGTCAGCCTGTTGTTTGGGCCCC

FIG. 4 (29 of 61)

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CTTGGCAGGGCTCTCCCCA GAATCTTCCCCTCTTGACTCCCATCANACA
GCACTCCANCTTTGTGTTACAGGCGATAAATGGGAAAGGGTAAAT
>Contig48
CATTCTTAATTAGAGAAACGCTCATTAACTAGACACCCAAATTCTCTGG
GGGGGGATCATTCTTACAAGCATGCCCTTCTCTCTTAAAGAGAGAGCACT
TTTTTCGCAAATAATGCTGCCATGAACATACGGGGTGCATGTATCTTCGT
AATAGAATGATTTCTATTTTGGGGGGTATGTACCCAGCAATAGGATTGCT
GGGTCAAATGGTATTTCTGGTTCTAGATCTTCGAGATCTTCCACACCGTC
TTCCACAATGGTTGAACATAATTCACATTCTTACCAACAGTGTGAAAGCAT
TCCTATTTCTCTGCAACCTCGCCAGCACCTGTTATTTCTTGACTTTTTTAA
TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTTGA
TGTGCATTTTGCTAATGATCAGTGATGTTGAGCTTTTTTTCATATGTTTT
TTGGCTGCAAGAATGCTCTTTTGGAGAAGTGTCTGTTTATGTCCTTTGC
CCACTTTTTAATGGGGGTTGTTTTTCTTGTAATTTGTTTAAGCTCCT
TATAGACTCACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT
GATATAACGGATAAAGAAATGTGGTACATATATACCATGGAATAGTATG
CAGCCATAAAAAAGAATGGGATCATATCCTTTGAAAGGACATGGATGAGC
TGGAACCATGATCCTCAGCAAACTATGCAAGAACAGAAAAACAATTGTTG
CATGCTCTCACTTATAAGTGGGAGCTGAACACTGAGAACACAGGGACACA
GAGAGGGGAACAACACACATTTGGGGCCTGTCAGGGGTGAGGTGGGGGAG
GGAGAGCATTAGGAAAAATAGCTAATGCATGCTGGGCTTAATACCTAGGT
GATGGGTTGACAGGTGCAGCAAACTCACTGTGGCACACATTTACCTATGTA
ACAAACCTGCACATCTGCACACGTACCCAGGACTTCAAAATAAAGAGA
GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTTGCAATAAAAACTTC
CTGCCCTTCACTTCACTCTGACTTGTCCCTGAATTCTTCTCGTGATGGT
GTCAAGAACGTGGACACTGGCTGGGGCTGGAGACTCACCAGCATCCGGAG
ACCCTCCTGAGCCCTCCAGCAATACAACCTTTGACACAACTATGAAATCA
CAGATCCAAGAAGCTCAAAGAACCAGCACAGGAAACATGATGAAACTA
CATGAAGGAACATCAGAAATTGAATTGTTCAAAATCAGTGATAAAGAGTAA
ATCTTAAAGCAACCAAGCAAAATATCCATCATATACGCAGAAATAAAG
ATAAGTATGACAGCAGATTTACAAATAGAAAAAAAACAAGTGCAGCAAC
AGAAACAACTATCAATCCATAATTCTATACCTAGTGAAAATTTCTTTCA
AAACAAAGGTGAAATAAAAAAATTATTTTCAGGAATACAAAAGCGAAAAA
ATTAATCACTAGCATTCACTGCAAGAAATGTTAAAGGAAGTCCTTTA
GGCAGAAAGAAAAATGATACAAGGTGAATATTTGGATCCCTGCAAGGAACT
AAAAAGATCCAGAACTGATAACTTAATGGGTAAACATGTAATTTTCATCA
ACAAGTGAATGAATAAACAAATCATGATATATCCATATGATAGACTACTA
CTTAGAATACAAAAGAAGAACTACTTATGCATGTGATAACATGAATGATA
TTCAAAATTATTATTGAGTGAAAGACACCAGATCAAAACAAAGTACATAC
TGTATGATTCTGTTTATATAAACTCTATAAATTGCATGCTCTTCTATAG
TGACAGAAAGAAGATCAGTGGCTGCCTGCAGACAGGAAGAGATTACAAAC
GGAAATGAGAATTCCTTAAGAGATGATGGACATGCTCATTACCCATCATA
TGATACAGCCATAATGGTTTTACAGATACATATATGTACACGCCAAC
ATAAATATAAGTTATCAAATTACAGTAAGTTCTGACTTAATGTCACTAGG
TTCCTGGAACTTTGACTTTAAGCAAAATGATGTACAGTGAAACCAATTT
TACCATAGGCTAATTGATATAAAGATGAGTTAGGTTTTTGGTTTTTTTTT
TTTTTGACATGAAGTCTCGCTCTATCGCCAGGCAGGAGAAGAAGAGTTAG
GTTTTACAGCATGTTTCTGGTCACAAGAACATCATCAAACCTTGTAATAA
AGGCACAAAACACTTCTAATATTAAATATCAAAATAAATATGAGTTATAC
AGAATTTAAGAAAGATTAATAAAAAACAAGTAAATCATTATTTATGGGAT
TTTTGGTAATCAGTGAGTTATGTGGTCATAGTGGAAGTGGGTTAAGTCAA
GAAATAAATGTTTGCAAAACAAAAATTTTAAAGATCCTCTCCTACCACCA
CACAAAAACAAGAAAACACGGTGGGCTCGCTAAGCACTTTTGTACCACT
CGTATCTTATGCGTTTGTATGATTATTGTAATGCTTTATGATAATTTTT
AGAGACAGGGTCTCACTCTGTGTCTCAGGCTGGAGTGAAGTGGTGCAATC
ATAGCTCACTGCACTCTCAACCTCCCGGATTCAAGAGATCCTCCACCTC
AGCCTCCAGTGCTAGGACTACAGTTGTGTGCCACCATGCCCATCTAT
CTTCTTTTTTATTTTTTGTAGAGACAGGGGTTGTGCTTTGTTGCCAGGC
TAGTCTTCAACTCCTGGGCTCAAGCAATCCTCCTGCCTCAGCCTCCCAA
ATGCTGGGATTTTCGGACATGAGCCAGCAGCACCTTGCCAGCATTTTATT

FIG. 4 (30 of 61)

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TCATAATAATTATAAGTCATTCCCTTCATTTCATCTTACAACCCACTTGTTTC
CAGTTTCAGGATCTCGGGTGACCAGAACCTATTAACGTTTCACGCACAAGTC
AGAAACCAGCCCTGGACAGGACACCATCTTACCGCAGGGAGAACTTACAC
ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACTTT
GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTTAAAAGACTGAC
CATACTTGAGTGTTGAACAGGATGTGACACAACCTAAATCTTTTAAGCGCT
TCGCGCTAAATGGCACAGCCGCTTTGGAAAACAGTTGGCAGTTTTTCAAG
TTAAATATACCCAACTCTATGATCCACTTCTCAACAATCAAACAAGAGA
AATAAAAGCAATGTCTACACAAAGATGTATACACAAATGTTTCATTGCAGC
CTTAATTATACTAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACCAGA
TGACTGGAACATACAAATTGTGGTATATTGATACAATGAAATACTACTTA
GTAATAAAAAAGAAAGAGCTATTAACATAAGCAACAACATGGATGAATCT
GAAAACAATTATGTAAGTGAACAAGCCACACAAAAGTTACATACTGTA
TGATCACATCTACATAAAATTACAGAAAAGGCCAACTAATCTATAGACAG
AAAAGCAGATGAGTGGTTACCTAGGGATGGGGCAGAAGGGACGAAAGGAT
GGATTGCAAAATAGCACAAAATATTGGAGGGATGACAAATATATTTCATT
ATCTTGATTGTGGGGATAGTTTAATGGGTATATATAGAGATCAAAGCTCA
TCTAATTATACACTTTAAATATATGTATTTTCATTGTGCATCAGTTATTCA
TCAACAAGACTATAAAATAATATATGCCTACATACATTTTAAATATTCA
AAATCTCAGGTTATATACATAAAATGCAACTGAATATGTATTTCAGATGTT
TTAACAAGCAGAAAGGACTGATTAAACTCATGACAGCGGCTGTTTCTGGG
AAGGGTGTAGGAGACAAGAGATGGAAAAGAGGATGAGAGCCAGAAGAGAC
CCTTGTAATGTTTTCTTTCTTTAGTAAAAATATATTGACAGTTAAAGCT
GAGAGGTGAGAATAATAGTCTCATGGCTTTTGTGTCTTAAATTTTACA
AACTAAGTGAATGGGAGAAAGCAAAAAATAAACTTAAATAAATGTTAT
ATTGCCCAAAAAGAGATTTAAATGGAGGTTAGACACATGAGACTTACGT
TCTCAAAAAGTAGAATCTGCAGGGAAGTTTAACTATAAAGAATTAA
AATCTAGCTTCTACCAGCCCAAAGCCTAAATGTTCTGCTTTATTCTTCC
TTATTATAATTATAGGTAATATATTTTATGTTTGCAAATGAATGCAGTG
ATATTAGATCTCTAAGAGGTGCTAAAAATGAAAAGTACATATTCCAATTT
TTCCCAATTTTCTTCTCTTTCCATGAATGAAAAATATACATATTTGATG
ATTTCCAAGTTTATACAACCGATCTTCTCTTAGTTTTCTCTTACCAAAT
TCCCTCCCTCACTCAGCCAGCCAGTCCAACTGTGCTACCTGCACAGC
AGCCCTCATACCATCCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG
AGCAGCAGCAAGAAGGAGACAGAACCTCCACGCTGAGCATCTCAGGGCTT
TCTCAGAGACTCCAGAGGACCCTGATAGGGACAGAGCCTGGCCAGCAATC
CATGCTGCCAGCTGTATGATTGTGGGCATGTAAATCTCAACTGAAAATG
GGTGTAAATAATAACATGTTCTTCCAGAATGAGCTTTATGAAGATCATAT
AGCTGTTTGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC
AACAGCCTATAAATAATACTTTAAGAAAGGGCATGAATGTAATTACTTAG
GAACAAAAGGCAAAGTGGAGAGATGCCTAGGACTGAGCTGGACAAGCTGC
ACCCTTTAGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC
CAAAGAAGGTGGAAGGATTCTGGGAGAGTGGCCCTCACCTGCCCAGGGC
AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGTC
GAGTCATGTGAGAATGTCCATGTGAAAACATCCACTGTGTGTATCTAAAG
AGAGTGGCTGTAAACAGGTGAGGTCAAAGGTCTTATTGTCTCAGATGT
TATCTGCATGCATTGTCTCAGACCAAGAAAATAAGGAGCATGGACACA
AAGGGTTAGGTTGAAGCAAAAATTTAATAAGTGAAAGAAGAAGGCTCTCT
GCAGTGGAGAGGGGAGTCTGAGTGGGTTGCCACTTTGACAGCTGAATCCA
AAAGCTTTTATAAGAACTCTTCTCATATCTGCAGCTGTTTGAGTAACTT
CTCTTACCTATAAACTGTCTGTATAACTCTCCCTTATCTATGCAGCTGT
GGGATGTCTCCAGGTAAAGCATAAAGTGTAGCTTCTCTGTTTGTATAACT
GTGGGTTTGTGTTTAGGCAAGCCCCCATCCCCCTCCCTGTGTAAGCTCCCAT
GGAGCCCAAGTGTGCATATCTGAGAAGTGGAGGAAGCTTTCTCTGGGAG
CTCACTGATCGTACAAAGAACAAGAGGCTTCTGTGCCGCTTATCTATTCA
GGTGCAGCCTGAGTTTTCCCAGGCTGCTCTATTTTGCCTGTAGCTATG
ATTTTTTCAGGCAGGCTGCTTCTCTGAAGACTAGCCTTAACTGTCTACCTA
TCAGATTTTCTTTTCTTCTCTCCCTCAGCTGGTTCCCTCACCAGGCTG
AGCAAGTGAAGAAGGAGGGCACAGGGCAGGCCAGTAGTGAGCAGCAACAAG
GAACTAAGACAGCAGAAACCACTTTTACACCTGGGTTGAAAGGGGTGGG

FIG. 4 (31 of 61)

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GAGCCAGGACTACAGC1 CAGGTAAGAACATAGGTAAAGAGATACTGTTGT
TGTGTTGTTTTTAACTATGAGAAGCATTGAGCTTTAAATTTCTACAGGAA
GGATCCAGTTTCAGACAGGAGCACCCAATATTGAGAAGAGAAGAACATGGT
GTAAAGGTCCTGGGAAGGCTGAGAGGATTGGGACTCAGAAATCCAGAGCAG
AAGCCGTCTGTGAACAGAAGAAGGACCTCCCCAGTGTAGCAAGAGGGAG
GGAGGAGGGACAGATGCCAAGATGGTTCAGGAAGAAGGTTTGGTGGTAAA
TGTGAGGCTGTGCTCACCTGCTGGCTTCAATTTTCTCTTTAAATGTCAG
ATGGAATCATTGATGAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG
GCATGGAGCAGCTCCAGCTTAGCCCGTGTTTAGGGTAATTATGGCTCCAA
CCCAGGAGATGAATATGACTAGGGAAAGTGAAGTCCAAAAACAAATGGTC
TCAAGTTGACTGTGAGTCTTCTGGGAGGCTGAGACGACAGGTGGGGTTGA
CAAGGGAAGGGGAACCCACCTGCTGAAAAACATCAGGCTGTTGGCTGGGG
GAGGGGTGAGGCCTGTGTTGTAGAGATGGATGGATGCCATAAGTTGGGTA
AAGGTTTCAACTCTACCCTCTGCTGGGTGTGGAAATAAAACAAAGACCACC
CAAATGAGAACAAACAAAGACTATTTATCCAGAGCTTGCTCTGACAAGGG
AGTCGGCAACCATCACTTGCTTGGCAGAGACTCAGAAGTAAGCAGGGGAG
AAAGCCTCATAGCAGAAAGAAGGGAAGTCTTCATGTATGCCCTGAGTGGC
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAACTAGAAAATGGGGGACTC
CTGTGTGATTGATTAGGAGCATGTTTGGCTTTCTCTGGTTGGTCCTACAT
TGGAAGAGGGAACAAAAAATTTAGGGCAGTTGTGAGTTATTAATCAAGTG
TTGGCCATTTTGTACTGACTGTTACAGGAGTGACTGGCTCCCTGGATTGT
TTGCTAGAAATAGTGGTCTTCACTTCCTGCAAGTCTGACTTTCTGGTAAT
AGGCTTCTGGGTGGCTATTGTGGATAATAAGTGGGTTTCTGAGCTGA
TTTCTGCAGATTGTGGATCAGAGTTATTTATATAAACAGTCTGACCATT
TTCCACTGGCATATCCATCTTCCAAGAGCTGGCCAAGCTGCTGTCTTAT
CTGTCTCCCCAGCCCCCTCCACTCTGGCTGTGAAAATACAAGCCACTAGG
TGAGGAATGGGGACAATTGAAGACTGAAAGCTTTTCTTTGCTGGGTTCCG
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGGCCAGTT
TTAGGACTGTAGTGGTAATGCAAGGACTGTGTGAGTTTATATTTTCATTT
GTCTCTCTAACTAAGGTGGAAAAAAGAAACAGAAAATTGTCTGTCTGCA
GTCTCTGCAAAAGTCTAACTGTGCTTCCCAACATTGCAGCCATTAGCC
ACAGGTGAGTATGAAAAGACTTTAAATGAGACTGGTCCAACTGAGATGTG
CTCTGAGAATAAAACACACAGCAGATTTCAAAGACCTAGTACATGCCCTG
ATTTCAAGCTATATTACAAAGCTGTGGTAATCAAAACAGTATGGCATTGG
GAAAAAATAGACACATTGGTCAATGTGACAGAATAGAGAGCCCAGAAAT
AAACCCGTGCATGTATAGTCAACTAATCTTTGACAAGAGTACCAAGAATA
CACAATGGGGAAAGTCTCTTCAATAAGTGGTGTGGGAAAACTAGATATC
CACATGCAAAAGAAAGAAATTAGACCCCTGTATTACACAAAACTTAAAT
TAATTCAAAAATAGAAAAAGACTTACATGTAAGATCTAAACCATAAACT
CCTAGAAGAAAACATAGGGAAAGAGCTCCTTGACACTGGCATTAGCAGTA
ATTTTTCAGATATAACATCAAAGTACAGGCAATGAAAGCAAAAAACAAGT
GAGAGTATATCAAACATAAAAGTTTCTGCACAGCATAAAACAATCAACAGA
GTAAGACATGACGTATGGAATGAGAGAAAATATTGACATCTGACAAAGG
GTTAATATCCAAATATATAAGTAATTCACACAACCTCAGTAACAAAAGCC
AAATAACCTGACTTTTTTTTAAATGGGCAAAGTACCTGAATAGGTATTC
CTCAAAAGAGACATACAAATGGCCAAGAGATGTATGAAAAGCTGCTTAA
CATACTAATCATCAGAGAAATACACAAATCAAAACAAGATATCATCTCA
CACCTGTTAGAATGGCTATTATTAAAAAATGAGATAAGTGTGGCCAGGT
GTGGAGGAAAGGAAACCCTTGTACATTATTATAGGAATGTAAATTAGTA
CAGCCATTATGGAGAACAGTATGGAGATTCCCTAACAAAATTAATAATAG
AATTACCATATGACCCAGCAATTCCACTTCAAGGAATACATTCAAATACT
ATCAGTATCTCAATAAGATACTTGCACTCCTATGTTTCGTTGCAGCGTTAT
TCACCATAGCCAAAGATACAGAAACAAGTTAAATGTCCATCAACAGATAAA
TGGATAAAGAAAATCAGGTACATATATATATACAATGGAATATTATTTCAG
CAAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC
TAAGTAAAAATCAAAGCCTGACACAGAAAGACAAATACCACATAATCTCAC
TTACATATGAAATATGAAATGTAAATTTTATGGAAACAGAGTAGAATGG
TAGTTGCCAGAGCCTGAGAGTAGAGAAAATGAGATGCTTGTCAAATCAA
TCATCATTGAATATATATAATCTATTGTCAATTAAATATTTAAGAA
TAAAAATACCTGGCACCAAAAAAGAATGCAAAATGTCTCAACAATGTT

ATATGTATTGCATTTTG..AGTGATAATAATTTGAATATTAGGTTAAATAA
AATATATTTGAAAAATTAACCTCACCTATTTCTTTCCATTTTGTGTTAACA
TAGGTACAAAAAATAAATTACCTATGTGGCTCATGTAGGTGGCTC
ACATTATACTTTGATGACACTATACAGGCTGGTGACCATATATCTCTTAG
ACTAGTCTAAGTGATTTAACAGTGGTTCCAGAAAGATCCAGGTTTAACAC
CAATGAAAGGGCCAGCTGGCTTAGCCAGCTTGTGTGGGAAATGTTGGGG
AGTGGTTTAAGACAGGGAAAAGCAAACCTTTTGATGCTATTGACTTTTTG
AAAAATCTTTTGTGGCTGAAAAACCAAACATTATT

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GCTCGAGTGTGTCTCTAAAGCCTTTCCCCCATTGGCTCCACTATACGCAC
TCTCCTGGTTTCTCCCCCTCTAGCCGCTGTCTTTGGTCTCCTTTCTGATT
TTGCTGCGTCTCTGTCCCCTGAATGATTGCTTCTCCACTACGGGGTGAT
TTTGCTCCCCAGGGGACATTTGGCAATATCTGGAGAGGTCTATGGTTGTG
TTTGAGGGTGTGCTACTGCCATCTAGTGGGGAGAGGCTAAAGATGCTGT
TAATGCCCAGGACAGTCCCCATAACACAGAATTATTGAGCTCAAAATATC
CATGTTGCCAAGATCAAGAAACCCTGCTCAAATATTAGCATGTGCTGAAG
GCCCTTCTCTTTCTTTAGCAATATCTGCCTCCTTAGGGATCTTTTCTAG
TCTCAGTGGTTTAAACATTTAAATCCCAAATTAGGCAATAAATTGGGCCC
CAAACCTCGTTAGTATAAAATGTAGAACTGTGTTATTAGAAGGCTAATAA
AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGGACCA
CGTGCAAGATAAATCCATCTGTTCCCTCTCTGTAATGTGGCGCTACCTTG
TGGCCGATTTTCTCGGGTTAAATATCTCTGGGGATGCAACTTGTCTGTG
GTTAATGGCTGTGTGAGGCCAGCGCTGGTGATAAAGGAATCAATCAAGA
CAATATTGAATTTAGAAAGGCAGATTTATTTAGAGAAAAGGAGAGATACG
TTGCAAGGGAGCAATGGGCAATACAGCAGAGGGAAGGCTGTCTGCAAAGA
GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGACAGAC
AAGATGCTTGCCTGCAGGTGGGCTGTGAGCTGAGTGCTTGGGTGCTAGTG
AGCCATTGGCAGCTGACCCTATTTCTTGGAAACATTGCTCCCTGCAAGCA
TTTTAATGTTAAACCGCCAGGTCAAGTTTGAATTTCTTTTCTTTTCTTTT
TTTTTTTTTTTTTGCTTTTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG
TAAATTAGACACCCTCCTGGTTTAAGTCACCGCTCCAGTGACTAGGCAGG
GAGCTCTTCTTGAAGAGGGTGTGGGCAGTGGGTACTTTGCATGTTGTCC
ACACCAGGCGAGCTGCTGCTTCAAGGCTTTCATTTGCTCTTTCTTTG
CCCCAAATGCACTTCTCTCACTGTTTACATGATTTTTCTCCCTCTTTTCC
TTTTAGTCTTTGTCTTAAATATCACCTTCTAGGGAGGCTTCCACACCAC
CTCTTCAAGATTTGAGGGTATGCACCCCCACCCCTAGCCTTCTTATCCCT
CTCCACTGCTTTCTTCTCAAAGCACTTGTACGTTCAAATAAAATAGATT
AGTTACTTTATAGTTCTAATTTTACTATTTTTTGTGTTACTTCAATAC
CCATGTAATCTCTGGAAGGAACGTTTCTTTTGTAGTGTATTTCTAGCAC
CTAGAACAGTACTTTGGCACATGGCAGGTGTTCAAAGTATTTGTTGATTA
TTTTCTCAAAGGGCATGGAGTCTTAGAAGTTTGAGAACACAGTTCTAAGC
ACAGCTGTTTAGAGACTATGGATGATGCTAATGGCTGTATTTCCAGTAGG
TGGGGCAATTTCTCAAATTGACCTGGAACTCTTGAGATCTGGGGACAGTCA
CCAAGCACTGGGCTCTGTGGGGAGAGATGTGCTGGTTTTTAGAGAGGAGA
ATAGCATCCTGGGGGACTTGGCCCCAGGGCTTCTGTCCCAATCTCTTC
CCAAGTGAAGTCCAGAGGAGGAGGCTTGTCTGTAGCTGGTCAGTCCTG
TAACTGTTTCCCTCCCATCTACACAGATGCAAAGAAGGCTGAGAAAAGCA
AGCTGTGAGGTGAGCAGGGGCCCTGACTCCTCCCAGAAAGGCACTCAGAA
CTTCCATAGGGCAACTGGAAAGAAGGTTCTACTTCTCACCGGCAGCTGT
TGCTGGGGAAAAAACCAGCCTCAGGCCCTACCCTGTGCTGAGAACCTGAA
TCCAGTATCAGGTTCTCCAACAACTTGGATCCAGCTGACCCTCACAAGG
GGTCAGATGCAACCTTGTAGCATATGGAAATGGCAGCAAGGTCCTTGTG
TGGACTATGCCTAGAATCTAAATTAAGACAAGGCCTCAGAGGGGCTAAGT
GACATCTGTCTCAAAGTTTACAGCTAGTGTGTGACTAAATCTTGATTC
CACCTCTCAGGTTTTACCATAATCCAAAAAAGGTTGAAACAAGAAAAG
TTATCTTTGGGCAATTACCTCTTTCTGTTCTTGTGCTTTACCTACTAATGT
TCTAGGCTCACCTCTGGTCTGCAATCTCACTGAACTGACAGATCCCTCA
TGGCCTAAAGGGTTTTCACTGGGTTGACTAGGCTCTCCCATGCTGT
CCTACTGTCTAAGGCACCTCCTGGGTAGGGTGCCAGCGTCATTCTGATG
CTGCCTGACTTTCTCCAGCTACTTTTGAACTTGGTATCCATGGCAGA

FIG. 4 (33 of 61)

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GGCTTAAAGGGCATGTTCCAGTACTTTTATTTCCAAATCCCCAGTGGU
ATCAAGGAAATCAGCATCTCTGGATAGCTCTACTAAGGCTTAGTTCTCAT
TGTCCAATCTAGCTCCTGGGTATGGGAGGCATTGAGGAAATATTTGAGT
GTAAGAGTGAGTTGCTTTACCTCCAGAATATCCTTCCAATGGCTCTGAAG
CAGGCTCTGGAGCTCCTGCTGGCTGATCACAGTTCACAGGTGGCTCCCAA
CCTGTGGTCTACATCCATCTCTTTGTGAGTGTCACTGCCATTGTCCCACAA
ATGTCATTTGGGCTAGCCCTGGGATAGTAATCAGTCTTTACATAGATA
TACATTGTGCTTTACATCCACAGTAATCTGAGTGGACCTTAAAAATAAT
TCCATGTGAGGTCTCACCAGCCCATGGGTTACAGATGGGGTTACCTTTCA
GCCTTGTAAGGTGCCCCGTCTTTGAGTGTAGACATGGACTCACAACGAG
CCACTCCTGCTGTTTCTCTGCTCTTGCTGAGGCTTCTGCTGCTGCTGCTG
CTGCTTTGACAGGCTGGCCAGCTGTGGTGCCTGAGGCACCTGTGTCTTC
ACAGCAACCAATTTGCATGAGTGGCCACGGTGTAGTTGGAAAGGGATGCTTA
GATGGGAGGCCAATGGGAGTCTGCTTCAGGAGGCAATCCAAGTCACAGAG
ATCGAGTCACCGAGAGCATAGTAAACTCAAAATCCCTTCTCTGCTGTTAAT
AACTGAGATGCTGTCACTGGGTAACTCACCAGCCCTGTTTGTGCTCTTC
ACTTAGAGTGATTTCTGTCTTAGAAGGCTCCTCATATCCTTCTGGGGAAG
GCTTCTAGTGAGTCCACAGATAGCTGGACCAGGCATGTCCAGAAATAATC
TGATTCTCACATTTGAGTTAGCCAGCGTTCCAGCTATATCCCCATTTTG
TGTCTATATAAGTTTACCAAAGCCCAAGGATAATTAGGTGGCTCCTTAGT
TTGCTTTATGATTATGCCTTGTGTGTGTGTGTGTGTGAGTGTGTACGCCCT
ATGAGGATTCTTCTCTCCCGTTCTTGCTATGGCTTCTCTTCCCCACTGA
TGGGCTGTAGTTCCTGTCTTTTTGACTTTGGGCTTAGTCATGTGACTTT
TTTGCCAAGGGAATGTGGGCGAGAAGTAACTGGGAGCCAGTCCCAAGCTAA
GGCCTTTGGGAAGCATGGTGAGCCTATGCCAGCTCCCTCAGAACTCCTTCC
CTTGGCCATGAAGAGAGATAAATCTGGATTGTACCTTCAGCCCATGTCTT
AGAATACAAACATGGGAGAATAATGAACCTTGAATCAAAGGCTGAAGGCGAG
CTGAGCCCATATGAGGTCAATTGAACTGCAGCTACCTACAGACGTGAAAG
TGAAATAAACATGTATAAGTCTCTGACGTTTGGGGTTTGTTTACATAGCA
TTATTGTAGCAGAAACTTAAATAATACTGGGGGCTAAATATAGTGGACCA
GTGACAGCACAGAATGGTAAAATGGAGTGATTGTTACTTACATCACAACC
CTTCATCTCTGTTGATGGACACTAAAATCAAAGTGGCAATTACTCAGAGT
TGGGAGTCAATTGAGTTGCATCTTGTGTTTGAATCAGTTGACAGTTTGA
GCTCTAAGTGATTACAGAGATGGTTTCTCAGCTACAGGTAAATAACAA
AGGCACAGAGAAGTAAAGTGACTTCTAGAGGGCTTCATTGATATTTAGCA
GCAGAATCAGAGCTAAACAATGAGTCTCTCATCTCCAGCCTTTCTATTCT
TGTTTTCTAGGTTGGGATTTTGGGAAATAGTGCAGAGAGATTAGCAGTAG
TGACATGGAAACAATGTGAGCCTCAGCTTCCATCCCTGAGGCTGCCTTCAT
CTGCCAGGGAATGTCTCTGTGTGAGCCCTTGCCTCTGACACAGATGTG
TATGGCCACCTGAATAAGTGTCTTTTCATAGCAGCTAATGGATTGAAATG
SGTGCTAGAGCAGTGCTTCTAAAAACTCCATGTATTAATCATCTAGGGGT
CTTACCAAAAACGCATGCAGATTCTGATTGAGTAGGTCTGGAGTGGGGCT
TGACATTCTGCACTTGTAAACATAGGACCACACTTTGAGTAGCAATGTAT
TAGATCATTCCAGTGGAAAACATGTATGAGTGATGGAATGAACAGATATAA
TTAATCCAGGTCTGGTAAGTGAGGTACTGATACATATTAAGTTGAAGTGA
ATTTACATCAAAAATAATGGTTACACAGTGACTTTACTGCCCCCAAT
TCTTTCTTTTGTAGTGGTTTCAAAGTGAAGTGCAGGCCAGCCGTTAAAGT
CCTGGTTTGTGTGTGATTAGAAGATTGATCCAGCTTTCTCTCTCTCTCT
AATTCTTTAAATATGCAATGGCCTTCTAGAACTTGTCTCTCAGGCTCCC
CATGAGCCACCTGTCTTAATATCTTCCCCCCAGGACATTTCTGGGTCA
AGGAAGGAATCAGGCACTAGGAAAAGTAGAAAGGTTGCCTGACAGTGAGA
AACTTTTTGCACTCCTATTGTTCAATTCTAAATCTGGGTATTGTTGGG
GCTTCTAATTGGAATCTAACTGAAATTCAGGCATGTCTAGCTATATATG
ACCAAGAATTAGGATGAGTTCAGTAGAAGCCTATTTTTCAGGAGAGCGGT
AGTTAAATTGAAGTTTATGGGTTTATGGTAATGGGTTGGGGAGTTTACTT
CATTAGCAATAGCAACGTTTTTGAATCAGAGAAGTGATTTTGAACACACT
GTACATAGTTTTCTCACTTAGATTTATCTCTGGGTCAACCTTTGTTGGAC
CTATATTAGAATCATTTAGTGAAGAAAGGTGGGTGTCATTAGGAAAAGA
GCCATTTATTCAAATGTTCTGTGTTGACATTAGGGCACTGGCAAGACTACA
GAATCAATAGATATTTAAAAACAGCCAGGTGCGGTGGCTCAGGCCTGTAA

FIG. 4 (34 of 61)

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TCCAGCGTGATTTGGC .TTACTTTGGGAGGCTGAAGCGGGTGGATTG
TGAGCTCAGGAATTCAAGACCAGCCTGGTCAACACGGTGAAACCCTATCT
CTACTAAAATACAAAAAATTAGCCGGGCATGGTGGCAGGCGCCTATAATC
CCAGCTACTTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCG
GATGTTGTTCATGAGCTGAGATCGCGCCATTGCACTCAAGCCAGGGCAAGA
ATAACAAGACTCTGTCTCACAACAAACAAGCGAACATACGAAACAAACGT
AACATCCAAACTAGCAGGTACATGCCGTGCCAGTCATGACCCATGGTCAT
AAGATGTCTACAGCTCAGGAAGCAGCTGCACAATGCCTGCATAGACAAAC
TCTTATGAAAGCAGAATGTCTGATGTCTCCATAACACATAACAGTGTAT
GCTTTTATTATGGTCATACTCTAGCTGTGATGTACCTACGCTCTAATATG
CCAACGATAGTTTCTTTAAATCATCAACATAATAAATGTTCATGCTGTCA
GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT
ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCCAGCA
CTTTGGGGAGGCCGAGGGTGGATCACGAGGTCAGGAGATCGAGACCA
CCCTGGCTAACCAAGTGAACCCCGTCTCTACTAAAAATACAAAAA
TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCCAGCTACTCAGGAAGCT
GAGGCGGGAGAATGGCGTGAACCCAGGAGGCGGAGGTTGCAGTAAGCCGA
GATCACACCACTGCACTCCAGCCTGGGGGACAGAGCGCAAGATTTCTGTCT
CCCAACCCAAAAANCNANNNNAAATTTGCACCCAAATCTGACTAATTTCA
GAGCCAAATTCAAATTTAGAATCGTTATATCTCCCTGGTGAAGTGAAGCTT
TTATCTTTAAGGAGACACACTCTTTATGTCTACCAATGCTTATGCTTAA
AAGTCCACTTTGTTCAGATACAGCTGCTTTCTTTTAAATAGTTTTTGTGTG
GTATATCTCTTTCCATCCTTTTTCTTTTCCAGCCTTCTCCATTCTTACATTT
TAGATATATTTCTTTTTCTTTTTTTTTGAGAGAGAGTCTCACTCTCTC
GCCCAGGCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCC
ACCTCCTGGGTTCAAGCAATTTCTCTGCCTCAGCCTCCCAAGTAGCTGGG
ATTACAGGAGCCACCACCAAGCCAGCTAATTTGTTGTATTTTTTAGAAG
AGATGAGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCA
GGTCATCCACCCACCTCGGCTTTCCCAAGTGTTGGTATTACAGGCGCGA
GCCACCATGCCAGCTGATTTTAGCTGTATCTCAAAAACAGCATGGGTTC
TGTTTGCTTTCTTTATTCAGCTTTATAATGTAAATCATTTACATCAAACA
TCTAATACACCATGGACTGTAAAACACAGCCATATTTTATGTATGAATTA
AAAAAACAACACCAATTAGTTCCTGAGACACACACCTTAACAATAT
CTCTGTGATGTGCATAAATCAATCACATCAGTTTTCTCTGCACCTCAAAAT
TTCTTTCTCAATTTCTCAGAGATATGGCAATTTCTCTGGTTTTACATTCC
CAGAAGCAAAGAAAAAGTACACAGCTTCTTCAAGTCATGAGTAGCTTCTT
TTTTATAGCTCTTGGTGTGTTGCAAAAAGATTGGAATTGCTTCACTAATA
CTAAATTTTCATTCTGCTGCTCTGTTTCTATGACAAGTCAGAGGGCATCT
TTTTGAAGACATTCTAAACAGCAATTAACCTCAAAACATGTAATGACAAT
GACACACAAAACCTCACTGATGACCAAATGAAGAGTTCCAGCCAAGTTGA
CACAAGCTGGCTGACAGAGCTTGTAAATACACACAGCTTGGCATATGCCTC
GCCATTTAGAGATGTAAAATAGGAATAAATGTTTTCCCTTAAATCAAT
GAAATAGAGCATTGGAAGTAAAATCTACGACAGTTATAGTGTCTTCTAT
TCATTATTTCTATTCTGTTTCTTCTCCCCCTTGCTTTCTTTAGTTTGAA
TATTTTCTATCATTTTCTTTTCTTCTCTACTAGTTTGAAACTTATGCATT
TATTTTCTATTTTTTAGCACTTACCTAAAATTAATCTGTAAATCCATGGAT
CCTTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTCTCTCC
CATCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCC
AACTTACATGCTTTTAAATGTATATATGTTAATACCGTATACCTTTTAAAA
CTTTCTAAAATAGCATTATTTTATAGCATGAGTGTTCAATTTACATTTTTG
CATATATTTAGAATTTTCTTTGCTCTTCTGTTTCTTCTTCTATTTATGACT
CCCCCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTGAAGCTGC
ACTATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAAC
TAAGTAAATTTAGTAATATTAATAAATCAGTTCTCTTCACTCTCACTAGCC
ACATTTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA
AACATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTC
TCCAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTC
ATGGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTAT
TTCTGCAACCAGTTACAGGGAGAAGGCCTGGAAATCATCACCAGGCCAAC
TCAAAATATGACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTC

FIG. 4 (35 of 61)

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TACGTGTAAGTGTGCAT CACCTGAAGACGTAAGTGATTAACCTCTTTTAA
ATCTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTA
AATTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCT
TGTCCTCTGCTAAATCATGGAGGTTTGGGGAATTCCTTTTAGAGCACCAT
TAACCTGTTTGTGAAGGCCTGGGAATTTCCCTCCAAACCCCCATTAAACC
TGTTTAAATCCCAAATTGGTTCCGTTAAATAATTCCTCCTTAATTTGTCCA
ATTTTAAAGGCCCAAAAAAGGCTGGGGCAAACCTCCTGAATGGCCTTTGTT
ACATTTCAACCTTTGTTTAAAAACACCGGTTTTTAATATTTAACTTAACC
ATTTAATCTCTACTGAAACACTTGTATATAAATCTGCATTAAATGAGAAC
TGGCCTGCGCCATATCTCCTTCTCAGAAATATCTTAGGGTTGTGATCCCCT
GTGTGAAGAGAATATATCTCTGGAGATCTCAATCTCTCTACCCCAAAAAA
AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCCACAGCGCTATCTCTC
TCCTCTCC

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GCTTGTCTAAGATGGTGCTCCTTGTGCTGTGCCTGCTTTCATCCTGGGA
TCTCCCTTCACCATCAGGATTGCCTTCACCTCATTCCAGTCTTGGATCTT
TCTTCTTGTCTTCTGAGTATTTTTTTTTTTTTTGTGCTGCATTCCCTTCA
GTGGCCTCTTGGGAAAAGATGTGTAGGGAGAAAAATTTCTTTAGAAACT
TGCATATCTGACAATATATTTATCCTATCCTGACATTTGGTAGATAGTTC
AGCTGGGTACAGAATCTAATTAATTTTCTTCTGATTATAAGACATT
GCTCCATTTTCTTCTGGCTTCCAATATTGCTGCTGAGAAGTCTGACACCA
TTCAAATGCCTGATTTTTTCCATGTGATTGTTGTTTTCTGTCTGGAGTGT
TGTAGGATTGCCTCTTTATCTACAGTGTCTGAAATTCATGACGTAGGT
CTTTCTTCATTCAATTATGGTAGACACTCAGTGGGCCATTTAATCGGGAAA
AACATGTGTTCTTCAAGTCTACAACTTTATTACTTCTCTTTTCTTGTG
TCTTTCTCTGGTCTGTTTTAGCCCCGAGTCTCTAGATCTGTCTCTAA
TATTCCTATTGACTTTACTTCTATTTCTAAGTCTTTATCCTTTTGCTTTA
CTTTCCGAGAGACCTGCTTAACCTTATCTCCCAACTCTTTTATTGAATTT
CATTTCTTTTACTATATATTTTTTACTTTGAATACACCTCTCTCTTCTC
ACATTTTCCCCCATAGTATTTTGTCTTCAATTGACAGTCTACTATCTTA
TTACTCTGGAGATATTAATAAGTTTTTTAAATTTTATTTATTTTATT
TTCAAAACAGTGTCTTACTCTGTCACTCAGGCTGGAGTGCAGTGGTGTGA
TCATGGATCACTGCAGCCTTGATCTCTGAGCTCAAGCTATCCTCCTGCTT
CAGCCTCCCAAGTAGCTGGAACCCACAGGCATGTGTACCATACCCAGCTA
ATTTTTTTGTTTTTGAGGTGGAGTCTCACTCTGTAGCCCCGGTCTGGAGTG
CAGTGGTGCAATCTGGGCTCACAGCAACCTCTGCCTCCTGGGTCTGGTT
CAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGAAACA
CACTACCATGCCAGCTAATTTTTGTATTTTTGTAGAGACAGTTTTCAAC
ATGTTGGGCAGCTGGGTCTGAACTCCTGACTTGTGATCTGCCCACTTGG
GCTCCCCAAAGTGTGGGATTACAGGCGTGAGCCACTGCACCCGGCCACT
AATTTTTAAATTGTTAATAAAGACGAGGTCTTGCTATGTTGCCAGTATG
GTCTTGAACCTCGTGGCTTAAGTAATCTTCTGCCTCAGCCTCCCAAAGTG
TTGGGATTACAGGTGTGAGCCACTGAATCTGACATTTTTTAAAGTTTTTC
TTCTCTTTACCAAGTCTTTTTTCCCCTTTCTGCTTTTTTGGGTGTTTTTA
TTTTGATCTCTATCTTGCTAGAACTTTCTGGAGACGTTTAGTAATACTA
GATTTTTGAGATGGGCAACTGGAAAGCTGATTGGAACTCTGAATACAT
GGGTGAGGCTTGTGGCTGTGAGTGTCAATTGCTTGATGTCCTGGCAAGGC
CAATGGGTTTGGGACCCCTACTATTAGTATAGGCCTGATTCCCTGGGAAA
GGCTCTTTTGATCTCCTGCCTGGAGGATAAAGGCCTGGCTACCAGCCTTC
TGTGTGTAATGTGAGGGAGAAGGGCTGGAGTATTCACATCATGCTGAAT
CCTTTCAATGATCATCTTGTTTTTAGTAATCTCCTACCTTAACCTCTCTGT
CTTCTGCTAGTATGGGAAAGATGACCTGAAATCTAACCATTTATTTTTTC
CCCCATTAATATCATTTTATGATTATTTCAGAAGTTAAATAATTGTCTATGC
TGTCCTCCAAAAAGACTGAATCAACTAGCAACAAATAAGAATTTTCTCAC
AGCTCTGCCAGCATTTTAAAGAATAGCTTTATTGAGCCCAGGAGGTCAA
GGCTGCAGTGAGCTGTGATTACACCACTCTACCCAGCCTGGGTGACAGA
GCAAAACCTGTCTCAAAAAAGAAATTTAAGGAACAGCTTTATTGTTGTA
AAATAGACATACAATAAACAGAGCACATATTTAAATTGTGCAACTTATAC
TTTGATATAACCTGTGAAACATCACCACAATCAAGATAGTGAATATAT
TTATCACCTCCTGATACAGTTTAGCTCTGTGTCCCCACCTAAGTCTCATG

FIG. 4 (37 of 61)

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CTGTGTGCTAAACCCGA₁CTGCCACTTCCAAGGAGTAGATGAGGAATG₁C
CATGGTTCTGGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTC
ATTTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGGAGTAACTCG
TCTGTACTAGGGCCCAGGAGAGTTACATGCTGCTTCCCATGTTATTCATC
ATTCCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGGCCTTTC
TACCATAAATGGGGGAATAAAATTCCCCTACCAGCCTGAGAAGTTTCTGT
TATAAAGAGGCTTTTTTTTTTGC₁GGGGGTGGGGGAGCAAGCCGACTAATGT
GTTATTTCCATACGGTTTGT₁TTTAAATGTAGATGTCATATGCAGGAGAG
GTGGTGTAGTGAGTCAACCGGATTAGAAGGACCAAGTCCGAAAAGCAGA
AGAGGGTCAAGTTCAGGGCACTGAGGACTACTGCATTCAAGTGGCGTGAAA
GGCAGATGGCTGAACAGGAGGGGGACATTACATTGCTTGTCTCCTTGAG
CCTCGATTTCCTCATCTAAAAAGAGGGTCATTTATTCACAGAACATTTAT
TAAACTTGTGCCAGGCACCGTGCCAGGAGCTGGACTAAAAATTAAATCCA
CCCCGTGAGCTGCTCTGAAGGCTAAATATGAAGTATGTAAAAGTAACC
AAGTGCTGTACACATGCAGCTATTCAATGACTGTGTGGGCATTGCGGCAG
ATTTTAAATTTTCTTTTTTATTTCTTTCTTTTAGTGAGAGGGTGTGGTTG
TTATTATTGTCTGCTGCTGTAAGTGTCTATTTCACTTGCTTTTTTGTGCC
TCCAGCCCATTCCAGGGCTGTCTAAGACACTTCTTATCACCTAAATA
ACCGGGGAGGCAAAGCGCTTTCTTAAGAGATGGATCCAGAAGAACATGC
TGGTTTTCTGTAGAAAAAGGGGCTGTGGGAAGTAGAGATAAGAAGGGAAT
TGGCCAAGATGAATGTACAGAGCCTTATTTTTTTTTTATAACACAGCAAG
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTTATAACTGGAAAG
GACCTCACTTTACAGGTGGGAAGAATAGAGTGGAGAAGTGAAGAGAATG
GTCACAGAGTCAATCAGCATGTCTGCGTCAAAGCTGGGATTCCCAATTCA
GGGCTCTTACTACAGTGACGTATGGCTAATATTTTGGCATTGTTTCGGGG
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTTTTGGGTGT
AACATTTCTGTTCTTGT₁TTTGTGGCCAAATCATAGTGTGATTGGGACAAGC
CACTGCCCTTCTCTGAGCCTCCACTTTCTTTTCTTCTTAAGAGGGAGGG
AATAGTAGAGTAAAAGTAGTCATTTTATCAAAACACCTGCTATTTTGGAGC
CATATTGCAAGTGGGTGGGGGTGAACACTTGGCTTTATTACCCATAGG
ATTAAATCCAACCTCGATACTGTGGCATTCCCAAACCTCCAGTCTAATCTT
CTTCTCCATCAGCCATGCCCCACGACACCCTGGTCATATCTGATGTTGCC
CCTTGCACTTGCCCCCTCCTTATCTTTGCTTTCTGACCTACCATATGGCT
ATTGGTTGAAATTCATTTTCCAGGGCCTTGCTTAAATATCATCTCATC
CATTAACATTTCTTGAACCTCCCCTTGCCCTGTTCTCCCTAATGTCTC
AAGCCAGAATTTATTTCTTTTGTGGCCAAAGGACTGGGTTTGTGACCTC
TCTCACGAGACTTAATATTGAGACCAAACGTCTTTAGACCTCACCAGCCA
GAGAGATGAGCATCTATGGAATGCAGGCTTTTGCCCTGGACTGTCTGATGC
AGGGCCTCTGCCTTCCCTCAGGGCCTCTCTGCTGTTTATAGGAATTTCCC
TCATGGCACAGTCCATGAGCTCAGGGTCAAGTTCATACATGTTTTACTT
CTTCTACTCTGCAATGGTCTTCTTGAACCTCTGAGGGTCTAAAGCTGCT
CTGCAGTTTGTGGGGTGAGTAGAAAGGGGCTTCAAAAGTTGTGCTGTTG
TTTCCCACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCCT
TGCTTTCTAGTCCCAACTTCTCTCTCTGAGGCTTTAAAAACAAGTCCCCT
AGGTTGAGCTGGACTGGAGTTGTATCCTATCTTCATTATCTGTCTACTCT
CTTCTGCTCTCTAGAGAAGATATTATATATGTGTGTATGTATGTGTA
TATATAATATCCATATATAGAACATATATTGTTATATTTACATATACATA
CATAACATATGCATGTATTATATATACATATGTAGTATCAAAGTTGGAA
TTAAACTGTATATTTTGTAAATTTGCTTTTATTTGCACTCTACTGTAA
ATGAATATTTATCCATACCGTAAGATATTCTTCAATGTATTTTTTTTTT
TTTGAAACAGGGTCTTGCTTTGTTGCCAGGCTGGAGTGCAATGACCCGA
TCTTGGGTCACTGCAGCCTTGACCTCCCCGGCTCAAGTGATCTTCCCACC
TTAGCCCTCTGAGTAGCTGGGACTAAAGGTGTGTGCTCCACACCCAGCT
TTTTAATTTTTTTTGTATTTTTTTTTTAAAGACAGGGTTTTTGCCACATTG
CCCAAGCTGGTCTTGAGCTCCTGGGTCCAAGCAATCCTCCCACTTTGGCC
TCCCAAAGTGCTAAGATTACAAGCATGAGCCACCAACCTGGCCTCAATG
TAATTTTTAATGGCTGTATAGTATTCCATCATGTGGTTGTACCCAAAAT
ATTTAACCAGTCCCAGTTTATTTCAATTTTTTTTACTATTTTGAATAA
TGTTTTAGTAAATACCCACAAATATGTACAATGGCTGGGCTTAGTGGCT

FIG. 4 (38 of 61)

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CACCCCTGTAATCCCAA₁ACTTTGGGAGTCTGAGGCAGGTGGGT₂CACCTG
AGGT₃CAGGAGTTCGAGACCATCTTGGTTAACATGGTGAAACCCCGTCTCT
ACCAAAAATACAAAAATTAGCCGGGTGTGGTGGCACACACCTGTAATCGC
AGCTACTTGGGAGGCTGAAGTAGGAAAATCACTTGAACCTAGGAGGCGGA
GGTTCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT
GAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAGTACAATTTGTTG
TACCTCCCTGATTATTTCTTTTAAGTAGAATTTCTTATAATTTTTTTTA
TAAGTAAAATTTGAATCAAGGGAGAAGCACCTGGAGTCCTTCAGATACC
TATTGCCAAACTGAACTTTTCTGTTCCAGGTTTACTACATTCAGCCTGAC
TCAGGGTTTGGGGAGTAGAGGAGGGGGTGGAGGCAGAGGGCCTCTCCCTG
TCCCCACAGACCTCCCTTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG
GCATTGCACCGTCAGGTCTGCTTCTCTGTAATTTCCCTAAATCCATCCAG
TGGAGCCTCATTTGTTCAAGTCTTTTTTTTTTTTTTTTTTTTAACTCCC
CTGAAGACGGAGTCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCACGA
TCTTGACTCATTTCAACCTCTGCCTCCAGGTTCAAGTAATTTCTCTGCC
TCAGCCTCCTGAGTAGCTGGCACTACAGGCGTGATCATCACGCCCGGCT
AATTTTTTTTTTGTATTTTAGTAGAGACGGGGTTTACCATGTTGGCCAG
GCTGGTCTCGAACTCCTAACCTTGTGATCTACCCGCTCTGCCTCCCAA
GTGCTGGGCTTACAGGTGTGAGCCACCAGGCTGGCCTCAAGTCTATTTT
TTAACTCCAGGAGGCTGGTATTTCAGAGGGATTAGGGCTGGCAGAAGGGC
CTCAAAGCTTTCAAGGCTGGGGAATAGGCTGCAGCCTGGTTCAGGGTAA
CCCAAGTAGATTTGGTTTCCAAAGGGACAGGAAAAAAGTGATTGATATGG
AAGTTGTCAAAGTGCAACTGTCAAGACATTAAAAATGTAACCTTTTAC
TAATATACAGTAGACTTGTGTTAAATATTTAACTGATTGTAAAAGGAAAA
AACCAGACCGAGTTTTCCCTACCATACTGTCAACAACCTCAACACTGAG
TTCTTCTGTGACCTCTAGTCACCGAAATGCTTGGGGATTCTCCCACCAC
TAGTCTCCAGCAGCCGACACCAGTTGGGTGTCTAATTCACCTCCAACAC
TATCTACCTGGAGTTAGCGTTAGATCCACAGGTTGAGGGCTCAGTCTCA
CAAGACTGCCTCCCACTTCAGGTGCCAGTTACAAGTGGTAGGTTGTCAAC
TATGCTTCTGACTGATGGCTATAAATCTGGGTTTGTCTCCCTCGGGTTCC
GTGAATTTGCTAGAGCAGCTCACAGAATCAGGAAAAACTTAAGTTTAC
CAGTTTATTCTAAAAGATATTACAAAGGATACAGATGAACACCAGATGAA
GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCATGCCC
CTCTGGGGCACCACCCTCCAGGAACCTTCATGTGTCCAGCTATCTGGGAG
CCCTTCCAAACCTGTCTTTTTTGGGTTTTTAAGAGTGGCTTTATTACAT
ACACATGATTGACCGAACCATTTGGCCATTGGTGAAGTACACAACCTTCAG
CCCCCTCCACTCCCTCCAGTGGTTGGGGAGTGGGGCTAACAGTCTCAAGTC
TCCAATCCTGCCTTGGTCTTTCTGTGACAAACCCCATCATGAAGCTACT
GCATTGGGGCTGCCAGCCAGCAGTCATCTATTAGCATGCAAAAGACACTC
TTATTATTCCAGAGATTTCAAGGGTTTTTAAAGCTGTATGTGAGGAAAC
AGGAGATGAAGAACAATATATATTTCAACATCACACTCGTTGGGGGA
ATTGACAGGATAGCAAACTGATTAAAGGAGGATAGGAGAGACTGAGATA
TATATTTCCATATATATATATAGAGAGAGAGAGATATTTCCATATATA
TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAAGAGTCTTTCC
>Contig51
ACACATTTGGGGGAGCAGTTCCGGAGGTACAGCCCGGACAGGAGATGTGA
GAAGATCGTGGTTANTGTTCCCTGGTCCAGAACCCCTCCAAGTGGGCTT
AAGTAGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTT
CCTCTCTGAGGGAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTT
TAATTATGTGCCAGTGGCAAGAGCGGGTGCTGAACCCAGGGGCCTGCCTC
AATCCGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATT
CCTTGCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTC
CCCAATTACGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG
CTCACAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAG
TGACGTGAATGAGAATAAACAGAAACAATAACCACAGCTGGGATGCTCT
AAGTCTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATG
GCAAAACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCA
CATTGTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCCC
TCTTAATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTG
TTCTTGGCTGTGCCTCTGGCAGCACATGCAAAATGGGCAGTAACAGTGGC

FIG. 4 (39 of 61)

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AGTCACAGGTAAGTAGTCTCACAGCTGGAGTTAAAGGCATGGGA
GAGACGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAAATGACCAGGGGC
TACTGGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCC
TGCAGGTGCAGTAGCAGCTTTCTGTAGTTCCTGATCTCTGGGTCCCACAA
TCTTCCCCGTTTTTGTCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTG
TGTGTACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCTG
ATAAGACATTGTCTGGTACGAACACAGTAACTCATTAAATCCGATATCTC
TATGAAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAG
CAGAAAAATAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGG
GTTGATATAACATATAATTATTTAGAAAAACATCTAAGGAAATAAAAGGCA
TAATTTAAAAATAAACTAGGCAGGTTTAAAAAATGAAGTAATCTATAA
GTAAAAAGTATAATTGTGAAATACATATCTTAGTGGATGGGTAAATA
GCTGAAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAAT
TCAGCATAGATAGAAAAATGGGAATTTACAAAAGTACACAGGAATTATA
AAAGAGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAA
CTGGAATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAA
AGAGGTGGCTGAGAATTTTTCAGAACCAACACAACTATGACTTTACCAG
TAGAGAAAAAATGTACACTGAGGAGGATAAATAAATACTATGAACAA
ATTGTAATAATAACTCAACAAAGACAAAGAGAAGATCTTAAATCAGC
AAAAAAGAAAGTCAGACTTAGAAAAGAAATGACAATGGCAGACTACTCAA
CAACAACATGGAACCAAAATTCAGTGAAACAGTATTTTCAAAATGCATA
TTTAATCTATCTTTGAAGAATAAGGGTGAAAAGGGTGAAAATTGCTGCCT
TATACAAAATATCAACATTAACAAAAAGTAATGAAGGTAATATAAAATG
TTTTCAATAAACAACAACTGAGAGAGTTTACCACCAACAAAGCATTCTTA
AATGGACTTTTAAATGCAGTTTTTAGGAAGAAGGAAAACAATTCCTAAGG
AAGGTCTGAGATGCAAAAAGGAATTATGAACAAAGAAATTTGTTAAATTA
TAGGTGAATTAAAAAAAGTGCCTGCATAAATGATAAATGACAATGATG
CTATTAATAATGAGTTGATAAGGATAAAGAAAAAGGACAGAATTAATAATC
TAGAAAAACAAGCATGCTGGAAAGGATTGAGGAATTACTTGAAGGTTAAAG
TTCTAGGGTCTTCTATCCTTCTAGAGGGGAGTCAATATATTAATTTTGG
ACCGTCACTTACACAGTGAAAAACTTTAAGGATAACCATAAAAAATAGA
AATAGAGAGTATAACTTCTGAAACAGTCAAGGGAAAAATATGGAATAAGA
AACTGACCAAAAAACATCTCAGTCAATCAAAAAAAAAAAAAAAAAAGAAA
GAAAAGGTTCCGAAGGAGAAAAATCAAAGCATAGAAAAAGCGGGACAAATA
GAAGTGAAAAAGAAAAAGGTAGAAGAAAAGGTCAGAAATATCACTGAT
GCACTAAATCACCATTAAAGATGAAAACAATGAACAACATCAAAAAAT
TCTAGTGAAGTGTAGTAGTGTGATCAGAATAGGCTCTAAGATAAGATGCA
TTATTGTGAGTCAACTTGTGATGATGAAAGGTTTAATTCACCAGAAAGAC
ACAATTATAAAGTTGTAATCAAATAGTTTTATTTTATTTACTTTATTTAT
TTATTTTTTTTGGAGACAGGATCTTGTCTGTGCTCAGGCTGGAGTGCAG
TGGCTTGATCTCAGCTCACTGCAGCCTCCACCTCTTGAGGCTCAAGCTTT
CTTCTGCCTTAGCCTCATGAGTAGCTGGGTCCACAGGCACACACCACCA
AGCCCTGCTAATTTTTGTATTTTTTGTAGAGATGGGGTTTCCCATGTTA
CCAGGCTGGTCTCAAACTCCTGGGCTCAAGCGATCTGCCCCCTCGGCTT
CCCAAAGTGTTGGGATTATAGGCGTGAGCCACGGTGCCTGGCCTCAAATA
ACTATTTAAGTGAACAAACTAGTATGGCCTAATGAAAAATGTATAAA
TCCATAATCGCAGAGGGATTTCAACTTACTTCTTTCGATTATGTAAAGGT
CAACAGACAAAAGACAATGACAAAATTAATGCAATGAACACTTTTGAT
TTAATGAACATATATTGGATATGTACCAAGAATTAGAGAATACATACTA
GTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTGGAAGCCTAAATT
ATAAAAAGTTGCTGTACGTAGAATAACACACAAACCCCTGAGTCCGGAA
TTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTTTATCCTCCACCA
CACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCTTGATTCAAATTC
CATGTTCTGTGAGTCAATCATTCTCTCTGCTGGAATAACTACTTCAT
ACATATTCTGCTATTGAATCTTGTCTTAGCACCCCATCTACTCCAAGAC
GATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTTGATTACACTTTT
TTTTTCTACTTCCATTATATTATTGATCAGTCTGTGCCACAGTTTTTGA
CTTTGTGTCTGCTTTTACTCTTTTCTAGACCCTGAGAGCTCCTGAAGGGT
TGGGTCAATTTCTTTTATTTGCTCATTCTCATGGCACAGTGAGTGCTT
AATAAATGGCTATTGACTGAAATTAAGTGTATCTAAATGGACATATTC

FIG. 4 (40 of 61)

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ACTTCTGGGCCATTCACTTTCTTTCTATTGGAACCAGGAGATGGGGAA
CCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACATGGAACCTTCCCC
TGAGGGCCAAAAAGAGCAGGGAAGGTGCAAAGACAAAATCTTCCATTT
TTAAACAAATGTAAGAATGTGGTCCACCTCATGCTCAGGTGGGACTTTATC
ATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTACCCCATATACAT
TTACCTTTAGTGAGGGAAGTGAAGACAGGAATTTTGTGATGCAGACTC
TTGCTAATGAGGCTAACACTTGGAGAAATTTTATCATGCATTCAAGAAGC
TTGTTTACATTTCTTCATTAATACTTTAGTTGGTGGTTAGCTTTAGTT
GTAGGCTTATCAGATATTTGGAGATATCTTCATAAACGATGGCTTTGGTT
TTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATAATCAAACAGCAT
GGCCATTTGTTTTGTAAGGCCTTTCTAAAATATGACGGTAAAACTACG
TGTGGAAAAATGCTTATTCTTCTGTCTCTATAAATGTGAATCTAGTTTG
TCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTCTAAGAAGATAAA
TGGAGCAAAGCACTCTGTGTTTTCAGAGTGTGGAAATCACTCATCCCTCA
TAAAACTGTCCCACTGATCCTGACTCACATGAATGAATTAATAAGAG
TTAATAACATCAATTTACATTTTTAAAGACACTTTCCCATGTTTTAGACT
ATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAGAGTTGGCTGTTT
TTGTCTGTCTGTTGTTTACGATTTTCAAAGCCATATCTAATTTTGTGCA
GAATGGTCTGAATTTCTACAAAATGTTGAGTTGTGTAGTGTGGAGAAGTA
CGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAGACCCTGAGATAA
GGCAGTAGTGGTGGCAACAGAGTGGAAAGGAGGTAGTTGAGATATGTTCA
GAGTAGAATCAGAATGGACATAGTGAACAACTGGATGCAGGTGGGGCTG
AGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGTTGATCCACTGAA
GTTACATTATTCAACACCACAAGGAACTAGGGGAATGAGAAGGCATACT
GGTTTGCTTTGGAGTGGAAAGGCGAGTGATGTAAGAGGAGTTAATGAGTTA
AAGTTTGGATATGCCTGAACCTCAATTTGATATGTGCATCTGATATACCC
TTGGGGTGACCCTCCAGGCAATGGTTGAACATGTGTATTTCTTAGTAAT
GATAGGCATCACAGACTCACATCAGTAAGGAAGCAACAGCAAACCTGATT
GGACGATATACCTGGAACCTCAGTACCCTATGACTGGAGCAAGTCTCTGTC
AGTGAAATGAGGATAAGAAGAATCTTGACCTTGTGGAATATGTTGTTAGG
AATATATGTGATGAACAACATAGGATACTTCTACAGGGCTCCACATGTA
GTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTGTAATTTATTTCC
AAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAATTAATAACAAAT
AGGACTGGATGCAATGGCTCACACCTGTAATCCAGCACTTTGGAAGGCC
AAGGCAGGAGGATCTTTGAGCCCAAGAAATCAAGACCAGCCTGGGTGAC
ACAGGGAGACCCTTGATCTATGAAGAATTAATAAATAAACCAGATGTG
GTGGTGACGCCCTATAGTCCCTGCTGCTTGAGAGGCTGAGGTGGGAGGAT
TGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATAATTGTGCCACCA
CACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAAATAAATAAATAA
ATAAATAAATAAATAAGTACAAACCAGCAAACACTAATCCTTTCTAGAGA
TTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGCAGAGGGACCTAT
GGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGGGTTGCTAGAGAG
GTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCAAGAATCCGTGAA
GACTCAGACTAATTTTTTTTTTTTTCATGAGGATTAGGTGTTCCTAGGA
ATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGTAGGAGAGCTGAG
GGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGCGTCAGTATGGCT
CACCTGCTTTCTTGATCTACTTAGCAGATGATCCACCCCAAGCCTCC
AGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGAGGGCCTGGAGCA
GTGTAAGGAAGACAGAGTCTTAAGAAATGCATTAACAGTCATGGTGCTT
GGCAAGTGTCGTCATCCTATGCCAAGCCTGATCTGAAGGGGTGCATGCTC
ATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCAATCCAGATCCA
TGCTCTCCTATATTCAATTTTCCAGGGGTTCTGCTCTCGACAGTGATG
AGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGTTGCCAATTTTC
CAAATGACAATGGGGCATGGAGCTTGAGAGTGGAAATGAGGCCCTAGGGA
TAGCGTGCTTAGGAAAACACTCCAGCCTGATGTAATCTGGGGGTACAA
TGGCATTTTTCATCATCAAGACTGATGTAAAGGGTGAAGTAGCAGTGAGTTG
GGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCCTAATCCAGACAG
AGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGGCCTCACTTAATG
TCCTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCTGAGGACAAGCTT
GGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGTGGCCTGCCCTGC

FIG. 4 (41 of 61)

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TGATGCCTGCCCTGCCATTCTGCGTGTGATGTCTCTGGGGCATCTTGCC
TTCCCTGCCCAGACCTGTAGTTTCTGAGGGCATGTGGAGGCCAAATGG
CTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGGGAGAACTGGAGG
AGCTAGCTAGTCACGGTAACCTGCAGCAGTCAAAGGATCGTCCCGGTGGAG
GTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTTTTCTTGGAGAT
GTGTGGGCATGTCTAGAGGAAATACCCAATTCCTGAGCCTTGAGCCCTC
CAGGAAACCTTGGAATATTAGGTAGTCAATCCCAAGGAAGTCTAAGAAT
TCTGGTCTCACCCATCTCCTTTAATTCCCAATGATCCTACATGATATT
AAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGTGGTGGTGAAGTT
TGACCTCATGATGGAGCGGAGGTGGTTTGAACCTAAGAATTTAATTTA
TTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCATACATAATTGAC
ACATAAAATTTGTATATGTCTACGGTGTACAATGTGATGTTTCGATCTAT
GTATACATTGTGAAATGATTACAACAAGCTAAATAACATACCCATTATC
GTGTTTCAAAGGAATTAAGCTCAAGCACAAAAGAGAGGTGCTGTTGAAGA
GTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGTCTGGATCAGGG
TCCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCTGCTCAGCTTCC
CCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACATGGCCACTTCT
CTGCATAGGCTTCTTCTCAACAGGACAGGGCTTGTGCTGCCCCATGC
CACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACACTGGCTGAGTGAG
GAAATCCCCCAGATTAATCTTGGTTCTAAGCATCATGGCTGTATTTACA
CGTATATGAATTACAAATTACAGCATAGTCAATAAGGATTTTGTGCTA
CAACTGGAATCCCAGATTATGCAAAATTGATAGTATAATTTGAAATTC
TAGGACTTTTATTAGTTTTAAAAAATTATACAAGCTTAGAGTAAGAAAT
TAAACAGTGCAAAAGAAATCACTGTGAAAAGTAAATGCTCTGTCTCTGC
TGAGAGACAGATATTGCAGCCCAGATACTACTGGGGTCAATAGTTTCTT
TAAGCATGCCATTTTGTATGGTTTATGGGACTTACAGCTCAAGAAGCTTGA
CACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTATTAGATATGACCG
TCTCATAAAGATACACACAGACACAGCGATTGGAGATATTCAGTGGG
CTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGTTGGGCTCAGAGT
AGCCTGGCATCGGCTGTGGGAGAAATGCTGGCATGGGGTTAGCAGGAGCC
CACTTAACATGTCTTAAGCCACCTGGAAGAGTCTTCAAGGAGACCAGAC
TCCAGAGGCCCTAAGGAAGGAAGGACTTTTGGCCGTTTTTAGGTATTCTA
GTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTCTGTGCCCCCTT
ACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCTGGCTCTTGAGA
AGACAGCAAAAGCGGGAATAAGAGGTGAGGAAGCTGTGTGGTTGTAGGAA
ATCCACAGAGGGCCTGGGGTCAAAGTGGTCATGGTAGTGACGGTGG
AGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATGGGCTGCTGGTGA
TCTGACCCAGCTCCTATGCTCTCCTGGTTTCAATTTAGGCTCTGTAGCAGC
AGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATATCAGGCAATCCA
AGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGCAGCAGCAGGTAG
ACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCAGATTTGTGTTTT
TAAGGACTTTTAACTGGGGAGCCCTCCATGACAGATCAGATGAGAGAGGA
ATCTGGGTCCGCCCATGTGTCAAGCTACCAGAGGGTCCCATCGGTGCTTG
GATCTTCTTGAAGCTGGGTCTGAGGTTTGCAGGTAGAGGGTGAAGTGGT
CAGAGGGACCTATTGCAGAGCTAACCACACCTTCCAGGAATGCAAGCA
CAAGCACCCACCGCGGGCAGGCGGGCAGGCACTTCTCCTTTTGCCACCA
GGACCTCACAGAGGCTGATCTGGCTCTGTGAGGTGGGAAAATGGGTTGTA
CTTAGTACATAGAGATAAAAGGCTTAGGAGGCCCCCTCCATCCTGTGACCC
TGTCCCCAGACCAAGGTGCCCGCAGGTGCTGCTATTTCAAGGCTGGGCC
TCAGTGCAAGCTTGTGGTTTTCTTGCCACCTGTGATGTCTCCACTAAT
GAAGGGGCTCTCCATCCTCTGTCTGCCTCTAGCAAGTGGAGGCTCTGGGC
CCTGGGCAAGACACAGGGGGAAATGCCATCTGTTATCAAATATATTTCA
ATGTGACAGGAAGCTGTCTTTAGAGCACAGC
>Cont1952
GCATGTGCTCTACATTGATCCAGGAGTTTGAAGACAACATTGCAAGACTG
GGCAACAAGCAAGACTCTGTCTCTACAAAAATAAAAAAATTAGTTGGG
CATGGTGGTACATGCCTGTGGTCCCAGCTACTCCTAAGTTGAAGAGGGAG
AATTGCTTGAGGCCAGGAGTTCAAGGCTGCAGTGAGCTATGATCACACCA
CTGCACTCTANCTGGGTGACAGAGCAAGACCCTGTCTCTAAAATAATAA
TCGTAATACATTTTTTTTTAAAGTAAACAAAAAAGGTCACTTTCTCA

FIG. 4 (42 of 61)

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TACCAAAATAAATTCCAAATAAATTAAAGGCTTAAACATGAGAAAGTTAA
ACCATAAAATTACTAGAAGAAAATAAAAGCAAATATTTAGATAATCCTGG
GGATAAATTTCTTTGGAATGAATTTCTTAAGATGAATCTCTAAAAGTGA
AATTCAGGGTTCAAAGGTCTTTCTTTGTCCTTTCTTTTCCCTTTCCCT
CTCCCTTTTCTTTCTTTCTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
TTCTTTCTTTATCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
TGCTTGCTTGCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
TTCTCTTTCTTTCTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTT
CTTTCTTTCTTTCTTACTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
TTCTTTCTTTCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
TCTTTCTTTCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
TCTTTCTTTCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
AACAGTCGCATGAACATGGCTCACAGCAGCCTTGACCTCCTGGGTCAAG
CAATTCTCCTGCCTCAGTCTCTCAAGTAGCTGAGACCACAGGCACCCACC
ACCAAACCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTTACCAC
ATTGGCCAGGCTGGTCTTGAACCTCCTGACCTCAGGTGATCTGCCTGCCTT
GGCCTTCTGAAGTGCTGGGATTACAGGCTGGGCCTCTACGCGGGCCGAG
ACTACCTCTCTTTAACTGGATCTCTGAGCTCTGGGCAGAGCCCACCCTG
AATCCTGGTCTCCAAAAAGGGAATTTATTAGGAGGCTAGACCATATGAT
GCTTTTACAGTGCACTTAAAAAAAGTTTGTTTTTTTTTTAAAGACATT
TCTACATGTCTAACTACAATCTTCTTGAACCCCAAGAGTAGCTTCTG
TTGCAATAGCTAGTCAAAATATAATAGTCAAAAAAATCAGGTAAACAA
CACAAACGCAAGCAGTTTAAAGAGCTGAAATGAACCTGTCTGTTTACACTC
TAGGGATTCCATAAGGAAAAATAGAAGTTTCTCCCTAAAAGGGAGCCTGG
CACCTTCTCCATTTTCTTTAAGGAACCCAGGCTATTATAAACTATTTTA
GGGCTCTCATGCAGCAGACGGTGCAAGAGAAAGGAGAGACAGCAGAAGTA
AATGAAGAAAAACAGAAATCCAGTCAACAGAGAAGAAAAAACTTTTGCTCA
AAAAAAGGCAAGTTCTAGGAAAGAAAAAAACATGAGGGCTATTTAA
ATACAAAGACGCATACATACACATGCACACATCTTGGATGTTAGCTTTTA
ATTAAGCTGACTTTTAACTATTGAGGTCCTTTAAAAATAAATCTTTTAAAA
TCTTATTACGATATTTAGCTAGGACAAATTGCTGCTATTTTCAACATTAC
CAAGTATCAAAACCAGAAAGGCTTGATTTAGGAACCAACCCAGGCTGTC
GTGGTAGGAAAAAAGGCAGAACGTTAGCTATGGAACCCACAGCATGGGGC
AACAGCCATTGCTCTTTTCACTATGGCCTGGCTAGCAAAAAGGTGGCCTTG
TTATGTAAATAAAGCCCGTTTGGTGGTCAAAATGAAACATCTTTTCTTTT
TTTTTTTTCTTTTGTGGCCGTTTTTCCCCCACCATAACCAGTTTGTGT
GTGTGGGAGGGTGGGAATTTAGCCACTTCAGAGGCTCATTCCCCATAAT
TTGGAAATTTCTTTTGGATTTGATCAAGTCAGATAGAGTAGGTCAAACCC
AATGGGAAAAAGACTGAAACAGCAATAAAAAACAGAAACAAACAGTTAAGC
AAAATGAATGATCACACAACCTTATATGATTACTGAGTGCTCTAATGGTAA
GGAGAAATTAAGACCAGCTGGTTGTTAACTTTAGCCAAGACAAAACCCC
AATTCAGCTACTTACCTAGGGTTGGGTCTCAGGCTGAAGACCGCTCACTA
CCGTTCTAGAAGCAAGAAATAAACTTGAACCTCGTCTTACCTGTGTAGCA
GGACAAGCCGCAGACAAAATCCCTCAGACACCAAATTAAGAAGGAAGGG
CTTTATTGGGCCTGGAGCTGCGGCAAGACTCACGTCTCCAACACCGAGC
TCCCCGAGTGTCATTCCTGTCCCTTTTAAGGGCTCACAACCTCTAAGGC
GGTCCACATGAGAGAGTCGTGATAGATTAGCAAGCAGGGGGTATGTGAC
TGGGGCTGCATGCACCTGTAGTTAGAATGGAACAGAACATGACAGGGAT
CTTCACAGTGCTTTTCTTATGCAAATAACCGATTAGATCAGGGGTGATC
TTTACCAGGCCAGGGTGTGTACCGGGCTGTCTGCTTGTGGATTTTCAAT
TCTGCCCTTTTAGTTATTACTTTCTTTTGGAGGCAGAAATTGGGCATAA
GACAAATAGAGGGTGGTCTCTCTTACCTGCGGGGAGTGAGCTCAAA
CTCCTTAAAGGAGTTACCTGCCTTCCATCATCAGGGAAGCAGGAAATCTT
GCCTTCTTGTGGAAGCAAGTAAACTTCAAAACAAACAAAGAAAAAAC
AGGGAGTTGTACAGCAAAATAAACTTTTGAATTTGACCAAATTTTGGGAG
ATCAGGAATCTCTGAAGGAGATGCTTTAGACCTCAGCAAATTTGTCTG
TTGGTTTGAGCCATAAAGTTAGCTCATGCTGGTACCAAACACCAGTAGGA
GATTTGTCAAAGGTAAGAGGCATCTCCTCAGAAATCCCTTCGTGGTTAC
CAACATGTGAACCTTGGAAATCTGAGACAGGTCTCAGTTAATTTAGAAAG
TTTATTTTGGCACGGTTGAGGACACCCACCCATGACAGAGCATCAGGAGG
TCCTGACCACATGTGCTCAGGGTGGTCTGAGCACAGCTTGGTTTTACACA

FIG. 4 (43 of 61)

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TTT TAGGGAGACATGAGACATCAGTGAATATATGTAAGATGTACACTGGT
TCCCTCCAGAAAGGCAGAACAACTTGAAGCAGGGAGGGAGCTTCCAGGTC
ACAGGTAGGTGAGAGACAAACAATTGCATTCTTCTGAGTGTCTGATTAGC
CTTTCCAAAGGAGGCAATCAGATATGCATTATCACAGTGAGCAGAGGGG
TGACTTTGAATAGAATGGGAGGCAGGTTTGGCCCTAAGCAGTTCCAGCTT
GACTTTTCCCTTTAGCTTAGTGATTTGGAGGCCCAAGATTTATTTTCTT
TCTACATCACTGTGGGCAGCTGACTAGGAAAGCTTTGTAGGACTGGTGGG
CAGTGTGAGAGCCCAGTGGGGGGTGGTGGTCTGTGCCAATGGTAGCAAC
CACCTGTGAGGCTGAGTAAACTCATTTCCTCAACCTCCTCTAGCAGCCCCA
GTGGAGATACAGATGAAGCAGACTAGCGATACAACCCAGCCTGAAGTTTT
GTCTGGTGAAGTGAATGGAATAAAAAATGGGAAGGGTGTGAAGAGACCAG
CAAGAAAATGGTTGAAGAGATGGGGCACAGAAATTAAGCTGGATCAAAAA
GGACGGAAAAGCAGAAAGGGCCGATAGAGAGAGGGGATATCTATGGGTTC
GCGATTCTGAAAAGGACAAATCACTGGTGTCTTTGAGAAGAGAGAGGGTGA
GAAAGCAGGAAGGCTGGAGGCTGTCTCCAAGAGGGCGACATCTGTGAAC
ATGATTTCCAAGATCACCAGACCATGGGGGTGGCCAAAGGGAGTGCCTCT
TCTCACCTCCTACTCTTAATTCCTTGTACTCAAGATAATAAGTTCCCGA
AGAGAAGTACCCATATTTAATTCATCTGTGTCTTCTAGCAGTACTAAAA
ATATTATATGAAAGGTATCAAACCTTTGAGAAATGTGTGCTGCTAAATTGT
TAAGGATGCTGGAAAACCTCAAGACGTCCCTGATCCTGAGCCTGAGTATGA
GCCTGTGGTGAGCCCAATGCAGGTCTCCATTGAGACAAAGGCCTCAGGGA
ACGGATGAGACCTAGGGACAGAGATGCATGCTGGAGCAGCAATCCCCATC
CCTACTGCAGCTCAGGCCAGCTGACTGCTTTATGAGTAAACGTTACCAGG
GAACACTTTGCAGTCTTAACACACATGCCACCTGTGACCACTGATCCCT
GTTGGGTGACCACTGACATCAGAGATTGATGGCAGCAATGAAGACAAGG
CTATCCTCATTAGGAAGGAAAGGAAGGAGGAGGGAGGGGCAAAACGAAT
CTTTCTGCTGTGTCAACCACGTCCATCTCTGTAGGTGATTTCCCATGTG
TGACTTTGTTTATCTTTATAATAACTCTGAGAGGTAGGTCTTGATGTCCA
CATTTTGAACATGAGGACATCCAGCCAGGAAGTTGAGTTCTGGGGACATA
GCTGAGAGGGCAAGCTACATATAAACCCCTCTTTGTTTTTTCTGGCTTA
TCCACTGAGTGCCCCCTGCAATCCACAGCCCATTTGTGAAGTGCACTACT
ATAGGTAAGTTGGCACAGGAGGAGTGGATGTGGGCGATTTGTGACAGCT
CTCCAGGAACCTTACACACTGGTGAGGAGGGCCAGGTATGTTCTGACCAG
TCACAATCAAAGCAACCTCCTACTAATCAGGGAGGCTTGGTACCTGGGGA
ATGCTATGTTGAAAGGTTCTTTCTGGGTTTTAAATGATGGGTCTATTT
CCTTATTCTTAAGATTGCTTTTTTTCTGGCTAGAACTTAAAGAAATTTT
CAGTAAATTTCCCTTCCCTGGCACAAAGTGAGCTTGAAATGAATTCCCA
GGTGGCCTTGATACTTTAAAAATATTGCCCTCTATAAAATCAACCTTTAGA
AGAAGGAAGTCAAAGAACATGCTAGATTTCAAAAGGTTAATTCCTTGAA
ATCCAGTTATCTACAGGACAATGTTGTCAAAGAAAAAATTATTTGGCCAG
GCACGGCGGCTCATGCCTATAATCCAGCACTTTGGGAGGCTGAGGCAGG
TGGATCACCTGAGGTGAGGATTCGAGACCAGCCTGGCCAAACATGGTGAA
ACCCCATCTCTACTAAAAATACAAAAAAATAGCCAGGTGTGGTGGTGG
GCACCTGTAATCCAGCTACACGGGAGGCTGAGGCAGGAGAATCGCTTGA
ACCCGGGAGGAGGAAGTTGCAGTGAGCCAAAGTTCAAGCCACTGCACCCCA
GCCTGGGCAACAGAGCAAGACTTTGTCTCAAAAAAAAAAAAAATTCAT
GATATTTTTAAATTCATGGTAAGGAAGATTTCAATCAGAACAGCACAGA
AGATATAGGAAACACTGCAATGGGACTTTGCGGTGGGGGAGAGAGATTGA
ACACAACACTACATATACAGCACGGGCAAGGACATATTCATAGCCAGGAAGC
AGAGCAAAGATCAGTGGATGCGAAATTACTAAGAGGAAACATGAAAAATA
AGGGAGCTTCTGCCTAAACCCACCTAACCGGATCCTTGCTGAAGACAGGA
CAGGGTGATTGGACACCACTTTGGGGATGGTGGAGGATGGGGAATCCAGT
GAGATTTCAAGGGTGATCAGATATTGAACATAGAAGGTTCTTGCTAAAAA
AGGAGTTTACAAGAAAGTGTAACAATGTGCCTGGGAGAAGGTTGAGGAGC
CTGACTAAAAATTTGGTCAAGCAGAGAATATTTGCCAAGATAATAGCTAAG
TCTTCTGACAAACAATAGATGCTAAGCCAGCAAGGGTGATGTGCTCAGAG
AAAGCACTGAGGGCTTATTTCTTTTCCCCCAATCTCCACTCAGTCAAGT
CTAGTCCCCTGTCAATGTAGCCATTTGTAAGAATGCAATCAGGCAGGGT
CCCATCTCCTAGTGACAGGACTGACTGAAGTTCTGCTGAAGAGAGTGGCC
TGGGGCTGACACCGAGATTTAGAGTCTGGGTTTCGCCGAGAGCTCAGT

FIG. 4 (44 of 61)

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GTAGTGGCCATGCCCTCTCTCCACCTGAACGCCCAGTGTGGGCAGGAACAA
CTGCAGCTAGAAGTCTGGCACTTACGCTGGGGTCTAAGACCTGCCTGATC
TGCTAACTAGTCTTGTCCCTTGGCTATAAACTGACGTTGGCACCTGGCCA
GAAAGATGAGCAAGAGATCTCTGACACACCTTTAAGTCCCTGTGGAGTAG
GATTATGTTGGGAAGGTCACTTCTTGGACTGAGCAGCAATTTGAGAAGG
AAGTCCCATGCCGAAGTGAGAGAAGGCAGGGAATCCTGCCTAGTCAGCTA
GAGCAAAACAGTCTGCAGGACGGGACCCAGGGATGTGATCCTCCCATCCA
AAGGCACTGAACTAAATGACTAAAATACTTTCCAGGGCTCACGTTCTTTG
AAGAATGGGACTAAAACCTAAGACAGGAGCCAGCAAGTGAGGACTTGGAA
GGAGATGGCTCATCTGATCAGCCTCCACTCAACAATTTTAATCATCCACA
CTGGCATGGGGACACAATATGAATAAGTTGACAGGGACCTACTCTGATTA
AGCAGTGGGCTAGTGCAGAGACCTGTCAGTCAAGAGTGGACAGGAGATGA
TTTCAGACAGTGAGAACAAAATTAACAGAGTCATGTGCTAAAGGGTGGCT
GGAACTACAGAGGAGTTTAAGACTCAAGAGGTCTGGCTGGGCGCGGTGGC
TCATGCCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGCGGATCACAA
GGTGAGGAGATCAAGACCATCCTGGCTAACGCAAGTGAAACCGCATCTCTA
CTAAAAATACAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGTAGTCCC
AGCTACTCGGGAGGCTGAGGCAAGAGAATGGCGTGAACCCGGGAGGCAGA
GCTTGCACTGAGCCAAGATTGCGCCACTGCCCTCCAGCCTGGGCGACAGA
GCGAGACTCCGTCTCAAAAAAAAAAAAAAGACTTGAGGGAGTTGTTTTATT
TTTGTCTTCTTTTAAGACAGGGTCTTTGTTGGGCGCGGTAGCTCACGCC
TGTAAGTCCCAGCACTTTGGAAGGCTGAGGTGGAAAGATCTCTTGAGCCCA
GGAGTTTGAGGCCACTCTGGGCAACATAGCAAGACACCGTCTCTACAAAA
AATGTGCAGGTTGAGGCTGCAGTGAGCAGAAAAACACCGCTGCACTCTAG
CCTGGATGACAGAGCGAGACCTGTCTCGGAAAAAAAAAGAAAAAGACA
GGGTCTCGCTGTGTACACAGGCTGGAATGCAATGGTGCAATCATGGTTC
ACTACAGCCTGGAACCTCTGAGCTCAAGCAATTTCTCTACCTTGGCCTAC
CAAAGTTCTAGGACTACAGGTGTGAGCCACCACAGTGGCCTCAGGAGAG
ATCTTAATAATAAAAGGACAAAATTCCTTGCATCCCTTAGGGGCAGGATT
GACACTCAAGGATCAGGCAGAAAGCCTGTGCGGAGTGGGATGAGCAAA
GAGAAAGGCTGAGAGTTGTGAAGAGGGAGATGCAGTGCCAGCTAGGACAG
GCCTTTTTGGGCTATGGGAGGTTTTGAGAGGAGACCCACCTAAACTAAC
CCATAACATTGCAGTGGGGACCTGTTGAAGTCATGGACTACTACCTGAAA
GCCAGAGAAATGGGAGGAGCCTTTCTCTGAGGAGGGAATCTAGTCCATA
GGTATCTTGCCACCAAATACATGGACAGGCCCTGGGGGAAGATGGTGGTA
GCCCAGCTGGAGGAAAAACCAATTTGCCACCTGAACTAGCCAGGGTAAGCC
ACCCAGGCACTGAGGGTGACACCCATGCATGCACACACAGAATCACACT
CCTTCCTATTATTCCTCAATTCAGGGGTCTCAACACCCATTTTTTTTGT
TTTGGGTTTTTTTTTACATGTTTTACATTTTATTTATTTATTTTGTGA
CAGGGTCCCACTCTGTTGCCAGGCTGGAGCACAGTGCAGTCGTGCAATC
ATATTAGATTGGTGCAAAAGTAATCACGGTTTTTGTGATTAAAAGTTTG
CCATTACTTTTAAATGATAAAAAACCAGATTACTTTTGACGCAACTTAAAA
GCTCACTGCAGCCTCAAAATTCCTGGTCTCAGGGAATCCTCCTGCCTCAG
CTTCCTGAATAGCTGGGACTACAGGCACATGCAATCCTACCTGGCTAATT
TTTTAAAAATTTTTTTTGTAAAGATAGAAAGTCATTTTGTGTCCAGGCT
GGTTTTCAAACCTTTGTCTTTGTGCCTCCCTCTGCCCTGTGCAAGACCTTC
TGGATGCCCACTAATGAAGACTTCCAGGGAGAGGAAAAAGTAAACATAGGT
CCCTGATCAAGGGACAGGGTTTTATCGACCACAAACAGCATGCCAGATT
CCACTGGCAGTCTTAGAGGTGCAATTTGCCCAAGTGTGTGTGGAAGGCC
TCTCCCTAGCAGTTGGTTTTATACACCAGCCACAGCACAGCATATTCTCTT
AAATTGTGAACATTTGCAAAAACCTCTGAGGACAACTATCATGTCTTGT
GTACTTTTGTTTTGTTCCTTCCCCTATGTACACGCGCGCGCATGCACT
CATGCACGCACGCGCGCGCGCACACACACACACACCCCTCAAAGTAA
TGCCTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAAGC
TACTTTCTTTGGCATAACCATCACCTTTGATTTTCTTTCTGGAACCTCCT
ATGTTCCCAGATGAATTTGGAAGCCCTCAGGAAACATTTCAAATTTGCT
ATATGGGAGAAATGGGAGGGTCTCTCTAGAAATTTACCTGCCACAGGTAT
TTCTGGTAAGACACAGCAAAGGTGGCACCACCCATTCCTCGTTACAATGT
CAATGCCAGTCACCTTCCTGTCCCATAAAACCTTTATTAAAGGTGCAGAAAT
TCCCATGGAAGCAGGTGGACACCATCTGCTTCCAGCCAGCCAGGGGAGCA

FIG. 4 (45 of 61)

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AGGTGTCCACTGTGCTTGTGGCAGGAACCTGCGCTTCTCTACTCTCCCA
CTTTGAGGCCTCTGGGGCTGGCCTGCTGCCTCTCTATTGACAAGGCTGCT
TACTGAGCAGTTTCATTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA
CTTCTATTTAAACCCAAAGATATTCTTTCTAAGGAAACGCTTTCTGTGCG
GGGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC
ATCCGTTTGGGTGGATGATTCACGGAGCACCACCATGAGCCAGTTCATG
GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGCATTGACAGCAAGGG
AGACAAGCAAAACAAAGCTGAGGTTTGTGAGGATGTTCAAGACTCACACA
GCACAGAGGAGCATCCACCACCAGCTTGGGAAAGGACTTGTATAGAGG
GGGTGAAGCATGAGCTGAGTCTTGAAAGACTAGAAATTAGCCAAACTACA
AGGAGGAGAAGGAGTTTCCAGTCAGGAAGAACAGGTTATGCAAAAGCACA
GAGACTGAAAGAATATCACATTCAGGAAGCTGCAAAATAGACAGGAAAGA
TTGATGCGTGGGATAGGAGAGGAGGGCAGGGGATTCCAGGTGGGCCCTGC
TTGCCACACTCAGGAGCTTGAAGTTATCCACAAAGGAGGTGTGGAACCG
TAATGAATGGGTTTTGTGCAAGGGCTTATGTCACCGATTGCTTTTTG
GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAAATTTCCGT
GGCAATCAGGAAAACCAATTAGCAGATGATTCAAATGGCCTAGGGGAAA
GGGAGGAGGACTTGGACTACCATGCAGCAGCAGAAATGGAGAGAAATAAC
AGATCCCAGGCACCTCAGGAAGCGCTCAGAATGAGCCCTTCAAAGAACTTA
TGGTAGGTGATGATGGATGGAGTGTGAGTCTTGGGATAGCATTGCCTGG
AAAAAFACTTTCTAGTTGAGACAGGGAAGTGGGCCAGCAGAAATGGAGGG
CTTCTTCTTTTTGCTTTAAATACTTTTATAATTTTGAACCTTTGAAAT
GAGCAGATATATTAGCAAAAAGCCTAAAAGGGATATTTTGAATCACTG
CTAGTTCTAACATATAACTTTAGCTTGCACACATCATCAATTAACCTTG
ATAGCGCCTTCTGAAACTATCATCCCAAATAGCAATCCTTGTA AAAACC
TATTTTGA AAAACGGGCCTTG TAGGATAGCCTCACAGATGTTTGTGGTA
GATTTTCTAACACTTAATGT CAGGGAGTGAAAGGAATCCCGTTAGAAGT
TGGAAAATTTGGAATCTTATTCAGTATGATTAAGTTTTCGGCTCACAC
AAAAGTTTAACACCTTTACACAATCAGACTCTCTCATTTTACATTGCTCG
GTAATTAGAGGAAATCAGTCACCCAGAGCCTGGGTCTAGACTTGCAAAA
ATGCACCCAAACAAATCCTGAGTGGCCTTGCTGAGGACTTCTCCAGAAGA
TAGAAAACCTCAGTTCCAGCCAACAAGGGGGAAGCAGCTGAAGAAGTGAAA
TTAACAAAGTCCTGGAAGGAAATGACCAAATCATCTTTGATTGTGTAATA
ACCAGAGAGTAGAATAACAGTACGACAGACATCATTTTGGGAGAGAAGCATTT
TATCATAGCTTTTGAAGAGAATTTTTCAGCATATAAGCACACAATT
CCAAGACAGATACTTTCAAGGGATTGTTTTGACG

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ATGTTNNGGTTTTGGGACCCCAATTCAAACCTTCATGTTGAATTTTAACTCTT
CAATGTTGAGCGAGGTCCTGTGGGAGGGTGATTGGATCATGGGGGTGGGT
TCTCCCTTGCTGTTCTCAATGATAGTGAGTGAGTTCTCACAGACCTGGT
TATTTGAAAGTGTTGTAGCACCTCTCCCCTTCATTCTCTCACTCGTCACTG
CTCCGCCATAGTAAGATGTGTGTGTTTCCCCTTTGCCCTCCGCCATGATT
GTAAGTTTCTGAAGCCTCCAGCTATGCTTCTCTGTACAGCCTGTGAAGAC
TGTGAATCAGTTAGACCTCTTTTCTTCATAAAATTACCCAGTCTCAGGTCA
TTCTTTATAGCAGTGTGAGAGTGGAATGAATATAGTGCCATATGTTTGTAT
TCCCAGCTACCCAGGAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGT
TTAAGGCTGCAGTGAGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGA
CAGCGAGACCTTGTTTCCAAAAAACCACCACTGTGTAAATGTG
TTCATAAAAGTGTCTTGCTCCACACCTGTCCCTATATATCTTATTCCTC
AGCCTCCGACAACTACTTTATTCACTTCTTATGTATCTTCCAGAATCAA
AAAAAAAATCAAATACAAGCACAGTGAATGTATTGCCCTTCTTCCCCT
CCCTTTTGTTACATCAGAGTTAGCATATCATAAATACGGTCTGCATTTTC
TCTTTTTTCAGCTATCAGCATGTTTGGAGAGGATTTCATATTCGTGAC
ACAGCATGTATTAGTCAGTCCTTGCAATGCTATAAGGAAATACCTGAGAC
TGCATAATTTATAAAGAAAAGAGGTTTAAATTGGCTCACAGCTTCGAGGC
TGTTCCACAGGAAGCATGGCAGCATCTGCTTCTGGGGAGGCCCTTAGGAAG
CTTTTACTCATGCAGAAGACAAGCGGGAGTGGATGTCTTATATGGCAGG
AGCAGGACTGAGAGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTT
AAACAACCATCTTGTGGGAACCTGTCCAGGAACAGCACCAAGGGA
TAGTGCTAAACCATTATAAGAACTCCACCCCCATGATCCAATCACCCTC

FIG. 4 (46 of 61)

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CACCAGGCCCCACCTCCAACATCGGGGATTACAATTTGACATGAGATTTG
GGCTGGGACACAGAACCACCAATACCAGAGTGCTTTCTCATTCTTTTCT
ATAGCTGCCTAGTATTCTATGTCCTTTACTTCATTTAGGCAGTCTCTTGT
TGATAGACACTTGGGTACTTCCAATTTTTCTATTACAAATGATGTGCA
ATGAATAATTTTGATCATTTTCCATTTACATGGGTATGTCCATCTGTG
GGATAAATCTCCAGGAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTG
TGATTTTTCATAGTTAGCAAATTTTGTCTATAAGGGTCATATCAATTTAT
AGTCCCACGCGTAATATTTAACAGTGGGGATTTCCCGACAGTTTGACCAA
CAAGGTCTGTGTAAACTTTTGATTTTGTCAATCTGATGGGAAAATAC
TAGTATCTCAAAGTGCTTTTAATTTGACTTTCTTATTACAATGTAAAGCA
TCATTTTACTCTGCCCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGA
CTGTTAAGATCCCTTGCCCTCTTGTCTTGTGGATTTTGTCTTTTTTTT
CAAATGTTTTGAGGCAGTCTTTACATGTGAAACAAGTTATCTCTTTATC
TGGGGTGTGAGTTACAACACTTTTCTCTGGCTTGTCTTGGCCTTTGAC
TTTGCTTCTGGTGATTCCCGCAATTCTGAAAGTGACTTTTTCATCATT
CATTCTTATACACCCATGCTCTTGTTCACGCTGGTTCCTCTAECTGAGGG
CTTTTTCTTTTCTTTTCTATCTGGGAACATTTTTTAGAGACAGGGTCTCA
CTCTGTCTCCACGCTGGAGTGCAATGGTGCGATCACAGCTCACTGCAGT
CTTGAACCTCTGGGCTCAAGCAATCCTCCAGTGTGAGCTTCCCAAGTAGC
TAGGACTACAGGTGCATGCCAGCATGCCTGGCTGATTGTTTTATTATTT
ATTTATTTTTGTAGAGATGGGAGTCTCAGTATGTTGCCAGGCTGGTCT
TGAACCTCTGGGCTCAAGCGATCTTTCTGCCCCCTGCCACCCAAAGTGCTG
GGATTACAGGCGTAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTG
TTTATCCCTTTAGGCTTGATTCTTATGTGCTTCTCCTCCCTCCTTCTGG
CTACTCCTCTTGTCTTTATCTTACTCTACTTGTGATGTTACCTTGTTTC
TGCTTATAACTAGCTGCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTT
TCATCTCTGTACTCCAGGTCCTAGTACATAGCGCTTGCTCAACAGATGT
TTGGTGCAATTGATAGATAAAATCAATGGTAGCTGTTAATACCAGTCTTGAC
TCCCTGCAGTGCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCTT
TCTGTTGAACAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGG
TGGCCAAGGATATTTGTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGG
GCTTTAGTCCCCCAAGAACTCTCACAGCCCTGTTTGTCTTTACTGTTTCA
GTGCAAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTTTTTTCTT
AGTGAAGTTTATTTTCAAGAACCAATTGAACAGTATGATATTTGCTCATTAT
AAATATTTCCCATTTAAATAATCTGAGCTTATATATTTTCAGTCTTAATTA
AAGGACTTGATTTAAAGAGAGCACACCAGTCCAAATTGAATTGATTCCAT
AGCTATTTAAAACTAGGCTCTTTTACAGACACTGCTACTTCTTGCCCCCT
TTGAATAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA
ATAGGGAAGCGGTTGCTCATCAGAAATGTGGGAGCGAATGACAGAGGGTTT
CTTAGAACCAAAATGTGGCGTGTTTCTGTGAGGCGGGCTTTAAGTGAGT
AGGAGAGGTGAGAGAGGCGCTGGCTCAACAAAAGGGCTGGGGATTGGCCCT
GAAAGGAGAGAGCTGACTGTCTGGCTGATGGACAGGAGATCCTCTTAGC
ACTACCTAAGGCAGGCAGTTGGGCATTGGTGTAGACAACAGGAAAGTCC
AGGCTATAGCCGTACTCAAAAACCTTTCTGTTCCCTTTCTGCCAGCCCTA
GGGATTGAGTCCACATTCAGCACAGGACTCTCTGGGTACAGCTCTCTTTA
GGAAGACACAAATTGCATGGTGAAGTCAGTTATATCTTGCCCGCCTTTGG
TCCCTCCCAGGAAGACGGGCATGTTTTCTGCTTGAGAGGTGCTGATGTAC
CAGTTGGGGAAGTGGGCAGACTCAAATTCAGCTTGTATTGATTCTAT
CTTGTGTAAGACAAATCGCTTTTCCATCTTCTTTGGGTAATTTTGG
GATCTACACTCTGCAGCGAAAGAGAAAGAATTTTTGTGGGGCAAGGG
ACAAAATGCTATGGGAAAGATGTTCTTTGGGTGGCCAGAAAGGAACT
GACGAGCAGGTACATGATCAGGAGCCACACTCCTGAGTTGTAAGTGGC
CCCCAACTTTCTGTGTGATTATTTAAAGAGCCCTTCTTCTTTTCTAAAC
TTAGTGCCAAATGCTGAGGAGCATAATGTAGGTGAGAATTTTTTTTTTTT
GGGGGGGTGAAAATTAAGCTAGAGCTTCTTGAAGTACCTAGTTTCCAGGG
GCTTTTTATTGATTTTTTCTTATGGTCCTAGAATGACATCAACTTGGAA
ATGAAGCTTTTGTGAGAAAGCTGGAGGTGATAGTGGTGGTGATTTTGGG
AGTGGAGTGGACGTGATAATGGGACCCTTTAAGTCATCTATTTCCCAAGG
TGTCTATCAAATGAGAGCAGCCCTAACAAATATAATCTGTTGGGGTTGT
AACTATGGTAGGACATAATAACATCGGCAAAATGATTTAATTTTCTGCAG

FIG. 4 (47 of 61)

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CAGGATTGAAGGTTGCAAGCAGTTAAAAATTATGTTAAATTTATTTACAT
TAATGCAAAATTGTCAAATAGACCTGTTCCAGCTTTTCTAGGGATGGG
GGCGGGGAGAAGGTGGTGTCTGGGAATAAGTGGTAGCAGGAGGCTGAGA
AGGGCTTCATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTA
TCATCTTTCAACACGCGCAGGACAGGTACAGATTCTTTTCTTGAGGCCAA
GGCCACAGGTATTTTGTCACTTACTTTCTTCTCTGTACAAAGGACATGG
AGAACACCACTGAAGAAAGAAGGGGCTTGTGGTTAGGGACACAGCAGT
GCAGGGTCACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTG
GTAGCCTCTGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGA
TAACCTGACTTCTCACAGACAATAGCAGGGTCATTTGTTGATTTAGGGT
TTCCCTCAAAGGCTTGAAGGTTTCTCAGAGCCTCATAGCAGTAGGAACG
GAGAATGAAAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGA
AGCCATTGTGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAA
CTTGATCAATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAG
AAATCAGGCACCAGAATGTTTTCAGGAACAGAGAGTAGCCCATGGGAAGA
AACTGGGAGAGGAGAGGCTGAGCTGGGAAAGTGGCTCAAAGAGAGACAC
TCATTTTGATCTTCTCAGTCAAGCAGTGTCATTGGAAGGCCCTGGGA
TCACTCTTACTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTG
AGAGCAAAATAGCTTCCCTTGAAGTGGCTGTCTTCAAAGTCAGCAGC
CTTAGTTGCCCCACTCCTGTGAGAGGCTTGGCTACTGTGGCAGCATG
CCAGGCAGATCACCACAGCTAATGATGGGTTACCGCACTTGAAACTTTT
GCCCTTACAGCGGAGAGATATAAGTTCTGTGGCGGTAAAATTTCCC
TACAAGGAACCACTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGG
AAGACTGGGGAGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTC
GCCTCAACCAACAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATC
AAATGACCCCATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGAC
TTGGGTGGACATGGTCTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGT
CACACTCCTGTTAAACAAATGCACTGGCCAGTGCAATCAAAATGTGCCATTT
CTAGGACCAAAGTTTGTATATTCTTTTAAATATTTTTCCTTGTGT
TGATCATTTGCCCTTAAATTAATTTTCTACTTGTGTTAAACATGGAGAAT
TAGCAAGCTGCCAGGAAGCCAGGCAGGGAAACCAGGATGTTTCCATTTAC
CTTGTGTCTCCATATCTGTCCCTGGAGGTGGAGAGCTTTCAGTTTCATAT
GGACCAGACATCACCAGCTTTTTTGTGTGAGTCCCGAGCGTGCAGTT
CAGTGATCGTACAGGTGCATCGTGACATAAGCCTCGTTATCCCATGTGT
CGAAGAAGATAGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAAA
TCAGAAGGGCAGGCCTCGTGAGGCAAGGTGGCAAAATTTGATTTCTTGGA
GGACACCTGAGCATATACGGTCAAAGTCTGATGACAAACACCACTAGGGAT
GAAGCTGGGAGTGGGGTGGCTAAGAACACTGGACCTGACACTATTAGACA
TGGGTTCAGCTTCAAGTCTATTACTGCTCACTGTGGCCGAGCAACAGAG
CTACTTAGGTAAATGGTGTATGGTCATAACACTAGCCACAGGGAGGTTA
CGAACCTCTGGTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGG
AGTTGCAAAATGTCAGTAGCCATCAAGATCTTCTTAAAGATAGTTTCCAC
TAAAGAGATGATTGCTTTGGTTTCCAGCCTTCTTGTGTTTGTCTCCCCGC
TGGGCCTTCTACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCT
GGGGCTTGATGACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTC
TTGGCTAACTACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCA
TTCTCCTGGAAGGTCTGTGGGCAGGGAACCAAGCATCTTCTCAGCTTGTC
CATGGCCACAACACTGACGCGGCTGCCTGAAGCCCTTGCTGTAGTGGT
GGTCGGAGATTCTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGG
TCCTGGAAGGAGCACTGCGGAGAGAGCGAGGGAGCGCTGGTGAGGTG
GTCCTGCCAGGAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAG
GAGGAAAGGCTTGAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTG
GGCCAGGCGTGTGCTCATGCCTGTAAATCCAGCACTTTGGGAAGCCGA
GGTGGATGAATCATTTAGGTCAGGACTTCAAACACAGCCTGGCCAAATG
GCGAAACCCCTTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGG
GTGCACCTGTAATCCTAGCTATTGAGGAGACTGAGGAAGGAGAATCGCTT
GAACCTCAGGAGGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTC
CAGCCTGGGCAACAGAGTGAGACTCTGTCTCATAAAAACAAAAACAA
AACAAAAACAAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAA
GCTCAAGGAGGTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCA

GA CTCAAGACTAGAAATG TGGGCTTTCTGACACCTTACAGGCTATTCTTTT
AGAATAAATCCCATTCTACTTTGTTTCATCTTTTGTACATGCCCCACC
TACACCATACATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTG
TCACACTATGATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATT
ACCTATGCTCACTCAGCAAGTATTCAATTTTCTACACTGTTCTTTT
TCCTTTTTCATAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGT
ACTTTTGTGAAATGTTACCACTTCTCTTATTTCAGAGAAGCTCCGTAT
TAAGGCTTCACTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTG
AAAGACAGTTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG
AGAATTTCTTGCCTGGAGCAGAGCCAAGCTACTGGAAGAGGCAATGGGGG
CAAAGGCCAGGCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAAC
AAGTTATGCCAGTCTTAAACTTCTAAAGAAATATGTTTTTAACAAGATT
GAGGACTGGATTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAAT
AAAGCCAGAGAAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTA
GGCTGATGGCTGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAG
AAGGGACAGCAGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAA
ATGACCACTTTGCTGCCCAAATGCCCTTAGCTACAACCTGAAAATATTTT
AACTGGAGGTTGTCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC
TTTATTTTTCAGATGAGGTCCAAAGCGGGTAAAATGACTTGTCAAGGTCA
AACAGCAAGTGAATGGTTTTCTTTCAAGTCTCAATTCTTTTTGTTTA
TATCATCTATGCTTTGTTGTTATAAGCTTCAACCCAGGTAGCAAAAACT
ATTCTACTCAAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTG
GTTTCAGAGTTTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAA
AAGGATAATCAAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAA
TGGGAAACATTATCACTACTCCTCCCCTGTCAACCAAGTGTGGCCACC
ACCACCAACGTTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAG
GTCAGCAAGTGGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTC
TAAAACAAAATACCATGGCATCAAAGTGGCCCAGAACTCCCTTCTTTGAG
CTTTCCTGTGTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTC
TTACCTTCATCTGTTTATGGGCCATCAGCTTCAAAGAACAAGTCATCTCA
TTGCCACTGTAATAAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACA
GGTTTATTTTCTTCTCTGTGTACAAGACTTGACTGTTTATAAGAACT
GCAAACAGCCTGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTCACA
GTGATATGCGCAGAACAGTCCAGAAGGCAGATTCTAGGCCCTGGCAGGTGG
GCACCCTGGGTGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCAGC
AGAGTCAGCTAAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTC
AAAGGGATTCTTGTATTGTGGGCTTGGAAATCTTTTCTCCCCATTTGCC
CTGCGAGGAAGCCCTTGCAACAACACATCTGGATAGCCTCCAGGTCCCAAG
GCTGGAGGGACTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGG
CACCTGTGTTGCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCC
AAGCACAGATAACACTCTACTCTTGAAGAGGAGACCTGCTCATGTTACT
GGTCTCAGCGTCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAG
CTCAGGTACTTCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAA
AATGAGTGACTTCCCCATGACGGCTACGTTTATGTGTGATTTCTCTCAGC
ATCCAGTGCTGGCAGTCTATGCAAAGAAATGATCTCTGAGTAAATGAATG
AATGTGTGAAAGAGAAGTCTTTGGGTCTAGAGAAAAGCATTGCTAAAC
CAAACCCCACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTT
GACACTAACCTTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCA
GAATATTTCCCGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAA
AAGCTGAGAGAGGGAGGCAGAGAGGAAGGAGAGGGAGAGACAGAGAAAG
AAAGAGAGAGAGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACA
GAGAGACTCCCTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGA
GCAATGAAGATTGGCTGAAGAGAATCCAGAGCAGCCTGTTGTGCCTTGT
GCCTCGAAGAGGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTATAG
CTTTCAAAGCAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTG
ATTTTCAATCAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGAAGCTT
CTTAGGGGAGGGGACTAATAAACTGAGATAATTCTCTGGTTTATGGAAGG
GCAAGGAGTAGCAAACTATGACACATTTTGCAAATGTATCACCATGCAAA
TATGCATTGTTTTCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAA
TACTGGATTTTCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGA

FIG. 4 (49 of 61)

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CAAAGTGAAGACACACAGATTTATACA.GCACATACTTTTCTTCATTCA
CTTCTTTGTACTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATG
GGTACAATGAAGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGT
CTCTACCTTGGGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAG
GAGCCTCTGAGGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATAC
GGTATGCAGGGTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAA
GCTCACACAACCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATG
GATGAACCAGATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGT
GAACTCTGAAAAGTGAATATTGTTTCTGTAAGAATATCCATCTGAGACT
CTATCTCTTGGTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACAC
CAGCAAAGTGCCTGCTCCAGGGTACTGCCAGGGGAGCCCTCCATTTGTA
GAATGAATGAGAGTCCAGGTATGAACAGTGCCTGGAGTGTAGGAACACC
CTCCTTTGCCTCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTT
TGAGACAGATCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCAGCATC
TCGGCCCCCTGCAAGTTCCGCTCCCGGGTTACACCATTCTCCTGCCTC
AGCCTCCCCAGCAGCTGGGACTACAGGCACCTGCCGCCACGGCCGGCTAA
TTTTTTGTATTTTAGTAGAGACAGGGTTTACCATTGTTAGCCAGGATGG
TCTCGATCTCCTGACCTTGTGATCTGCCCCCTCGGCCTCCCAAAGTGTT
GGGATTACAGGCGTGAGCCACCGTGTCCAGCCTGTAACACTTCTTATAGC
ACTGAGTTGAAACCTTGCTCCTCCTGGTTCTCCAGGAACTGAAATCTT
TTTGAGCCAAGTCTAGCACAGTGCCTGGCATGTACATTGAGGTGGTAGAG
TTTGCTGCTTGAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAAT
TAGTATGTGCCAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGC
CTCTGTGCAAGTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAA
AAGAGCATTTCATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTTAATTT
GGCTCCCAGTATCTTGATATCAGGAGTCACTCACAAGAACTCCATCTTTA
GTAAGTTATATTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTT
TCCTGTGAATTTGATAAGCCATAATCCATTCTAACACTGAGCCCTCCTG
AAATTTGGTGTCTGGTCTGCGATAGCTAAAAGCCCTGTCTGGGTGGCC
TAGGGGACTCCTCTGTTTTGCCTCCACAGGATCCACTTTGCAAATTAACC
ACTGGTTCTCCCGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTC
TTCTTCTCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT
TCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTT
TCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTT
TTTCTTTCTCTCTCCCTCCCTCTCTCTCTCTTTCTTTCTTTCTTTCTT
TTTTCTCTTTCTTTCTCTCTTTCTTTCTCTCTCTCTCTCTCTCTCTCT
TTTGTCTCTCCCTCCCTTCTCTCTCTCTTTCTTTCTCTCTCTCTCTCT
CCTAGACAGGATCTACCTTTATCCCCAGGCTGGAGTGCAGTGGTACAAT
CATGCATTCAATTGCATGATCACAGCAGCCTCAAACCCTTCTCAGAGTCT
TTATGCGGCAACCAGCAGGGTCTGGAGGGTTGGTGGCTCTGTGAACCTC
CTGACAGAACACAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGA
ACGAAGGAGGATCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCC
GAGCATCAGCTCTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAG
GTCAGAAACCTTGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAG
GACCTCAGAATCTGCCAGCTAAGAGGAGCCGTAATGATTGTCTGGTGGGA
TATGGTGGGACCACAGAGATGAAGACATGAATAGCTATTTGAATGTGAAC
AGCAGACGAAGAAATCAAGGCTAGGAGGGTGAAGTGACTCATCCAATAG
CACAGTGTGGTTGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCTGAT
GCTTTCCGCTCGAGGGAAATTTGGAGCCATGGGGCAATGCCCCCTGACGT
AACAGTCTCCACAGTCTGCCATGTCTCATCCTGGCCCTGTAACCTGGAC
CCAAATCTGCTACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTC
AAATAGGTTGTGCAACGTATGTATCAGATCCTGTCTTCCAAGGAGACCG
CTCAGGCCACAGCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCG
CTATAACATAGTTGGCACTAAGGGAGGGAGTGAAGAGTGATGATGATG
TAGATGGTGTATGTAGCCCCAAGGAAGTGAACAAGCAGAGATGGGGAGCT
GGAAATGCCAGGATGCTCCAGCTTTTGGGGAATTATTAGCTCTTGAGTC
ACTAAAGCCTTTCTCAGCTGCAAGTTCCTCTTTACCCTGTCAGGTCATT
TTCCAAGACAGGAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATAC
CATCTTGTGTCTAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTC
ATCTCATTTGGTCTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCA

FIG. 4 (50 of 61)

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TGGGTTAGTTCTTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTT
GTAGTGAGCTGTTCTCTTCTGTTACCCTCTTGCTTAGAACAGAATAA
GCAATCTGCCCAACATTTCCCAATTTCCCATCTCATTCTTGGCACT
GGCTTCTAATATTTGTTCTTATGAGTCATTTTCTTGATCATTTCATG
AGTCCCTCTGGGATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCT
GTCTTTGTGGATATTTCTCTCTTCTCCCTTCTGCTTCTGGGATTATTTGG
GAATGGGCACTATGATTTTATCATATCGCTTCCACTTCTTTTATGGCAT
CATCTCCAATGGGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGG
GACATGCAGAGTCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAA
GGAGGGCTTAGATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGT
CTCCAATGGCTTTTCCCTGATGTGGGAGTTGTTATGTGAGTTCTGGGAGA
CCAATAAGACCTTGTCTTCTCTTGGATCCATCAGAAAAAGCCCCCTGGGT
GGGTAAGATGGATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCT
AGTGGGTATAAGAGAGGGGGACCACAAACAGAGGGGGCTCTGGTACCACTT
ATCCAGGGTCTGGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTT
AGGTACAACCTACTCAACCTTGCATCATTTCAGAAAAGCAGTCRGATAATA
CATAAATGAATGGGTGTGGCTGGACTTGTCTGCGGTCCCCCTGTCTTATA
TCATTGTATTATATCATTTTTTTCTTACATACAAATTTAGAAGCAATACTT
AAAAAAAAAAAAAGCCGCTCTTTATTGAGCACCTACTAAGTGCCAGGTACCT
TTTTTCCCTCATTATCTTATTAACCTCTTATAATAACCTTTAAAGTAGA
TAATATTGAACCATTTGACCTATGCAGAACTGAGGTTGAGACAATAAAT
TATTTAAGACCGCACAAACAGTAAATGCTGGAACCTACGACTCAAATATGG
GTTAACTGAACCAAAACAGATCTTTATTTCTCACTTTTAAATGTTACAT
ATGTTTATGGCTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCT
TTCTCATTCTCAGTGATTGAGTGACATTCTAACTACATTGGCCTGGCAG
ATTCACCTCTGTCCCTAAATGTTTCCACATTGTCTTTTAGGATTGAGA
TCCTCTCTGTTCCCTTGTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTG
CTGTGTGAATTTGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCA
AATCAGGGTTTTTAATGATCTCTCTCCTTTCTGAATTTCTTCTTAT
TCCCATTCACTTTCTCATCTATAAGTGGCANCTTTGTTGCTGGAAGATAT
CCCTTGTGCAGGGATTNCTCTTTAANAATTTGTCNNNACC

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GTGATCGTCAACCTCCACCCCTGTAGGGCCTCAAGCATTGAGGACAATCA
CTGGCTGCCCATTAACCCAGAAATGTTGCCGAGACAGGAGGCCGTGGCCC
AAGTTTCTGGAATGGGGTATTATTATGTGACACAAAGGCCTTTGCACAA
ATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATAGG
ATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCCTTGTCTCTGTT
AAAACTCACATCGTACGGCCCAAATAACAACAAAAATGGATGTAAATTC
TTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGCCA
GAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGAGG
ATGGCCAGTGACNTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGAGC
AGCAGCTTCGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTGGG
CAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCAGGTGCTGTCTGT
CTCCTCGTGTGAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTTGCATTT
CTTTATTTTTTATATTTTTTTTAAATTTTTTAAATTTTTTATTTATTTTA
TTTTTATTTATTTATTTATTTTAAATTTTTTTTAAATTTTTTAAATTTATG
CTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATACGC
ATACATGCGCCATGCTGGTGCCTGCACCCACTAATCGTCATCTAGCAT
TAGGTATATCTCCAGGTTAATCCCTCCCCCTCCCCCACCACCAAC
AGTCCCAGAAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTGA
ATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTTCAAGAAAT
TCAAAAGAGTATCCTTGGGAATGACTGGAATTCAGAGTCATCTGGTAAT
CCTCATAAAACAACCTCTGGATGTCTCTCAGCACATCTCCACCTTGAAC
GCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCACTTTTTTTT
TTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCATGTAAATAAATCAA
CTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAAG
GAACCAAAAGGCTTTCTCCCCGCCAACACACACATAACACACACACAAA
ATCATAAAAAACATACATACCCCCAACACATAACAACACACACACACA
CAAAATATATACACACAACACACACCAACATGCCACAAACCTGTGTCC
AAAAATAAATCCTACTGGTGGGTTTGTGGTCTCCCTAATTTCAAAATGA

FIG. 4 (51 of 61)

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AGCCGTGGACCTTCGCAAGTGAGTGTTACAGCTCTTAAAGATGGCATGGAT
CCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAAG
CTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGCC
AGCTTTTACTTCCTTTTGGCCCTCCCATGTTCTGTTTCCATCCTATCAG
AGTGCCCTTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTGC
TGATTGGTGCAATTTACAGAGTGCTGATTGGTGCGTTTTACAATCCCTT
GTAAGACAGAAAAGTTCCCTGATTGGTGTGTTTTACAATCCTCTTGTAAGA
CAGAAAAGTTCCCAAGTCCCACTGGACCCAGGAAGTCCACCTGGCCTC
ACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA
CATAACAAAAGTATACATGCATCTCCCAATATACACATACCACAGAAA
CATAACACAGGAAGTCAAGTACCTGTCAAAAGTCTGCATGGTGATTGCC
TCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTCAATAAATTGGAGT
CCTTAAAAATCGTTGTAAGATAGAAAATTTTAAAAGTATATAAAATAAA
ATAIGTATGTCCCTTTGGTCTAGCATTTACACATGTAGGAATTTATCCTAG
TGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCACA
GAATTATGTATGCATATGTGTGTGTATATATATATATCTCATACATAT
AATAATGTAAAAGTGAATAAATACTCAGATGTTCAAAATTGAGGATTAGTT
AGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTCT
CTCGAGCTTCAACCTCCTATAAACAGTGTCCCTTGTATATCAGTATTGGT
ACAGATAATCGAAGCTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGAG
TTTATGAATACCTTACTACACTAGGTAGCACCCTTATTAAAGACAAA
CTCTTCTCTCTCATTTCCCTTCCCTTCCGGAACCACTTGGTTGAATCTCT
ACAAGTCTCTATTGCAACTGCCCTCAACATGGCACCTCCCTGCATCTCCA
TCTTCCCTGTCTGAGAGCAATGGCCTGTGCCCCCACTCACATCTCTC
ATTCAATCCAGAAGTGAGCACCACAGAAGTGCCTACAGTTACCCCAACCA
CCTTCTTAGAAGATAAGTTAGTGTGTTTGTGACTTTTTAAAATTTTAC
TTCTCTTTTTCTTCAATCTCATCCCATCCCAAGAGGTTTATCAAGAA
GTTCTCTAAAGATATGTGTCTCTTATGGAATTTAACAGAAATCAGGGAT
TTGTATTCTAGCCATCAAGGGAATAACATTTTTCCAGGTCTTTAGACAAA
TAATGGAATACCTTGCAAGTAATTAGATACACTATTGTAGAAAAGTATTGA
TGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGATA
CATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTGAGACACACTCCTA
TATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAGA
CCACAGTCTTCGGTGAAGTTTAAAGAGATGAGGCTGCAGCATGCTCAGAAA
GGCCTGGGTATAGTTCTTCCAGTAATTAAGGATGTGATCTTGGGTAAAT
TGTCATCTCTCTAAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGA
TGGTATTTACCCCAAGGTCATCAAAGGATTTGGTTGGAGAAAAATAAAT
AAATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTAT
TGTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCC
AGAAGCTATTACCTTAATTGGTTATGTGGATTTCCCCTCATACTGAGCAG
CTGTGTGGTGTGTTAAACATAGCCATACACAGTAACGTACAAGGGCA
AATGTGATGGAAAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGT
AGAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCCTTTTGCAT
GTCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAG
TGTAACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGG
GACTCCACTTGCATGAAGTCTGGAATTGGGGCAAAGAACCATCATGAGAA
CAAGGGCTTCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCTGTG
TCCCCTCTTCTTCACTCTCTCTGTTTTCTATACCTGTATTATTGGAC
TGGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAAT
AGGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAAGGAATTTGT
TTATACCTTTGGCATGGAAAATAGCAGGAAATGAGTGATCACTGATAACT
GAGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGTATTGTCAT
AACCCTCACAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTC
AAGTAAAGGATCTTGAGAACTGAAGGCAACAGAGCTCCAGGAGTCCAAG
ACAGAGCCACAGACCAGGAGTCCCTGGCCAGGTAGGTGGTCTCTCTG
CACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTG
GCCATCTAGACCCTTGCTTTTTATCCCACTGGAAGCACATCTGAATTC
TAAATATGATCTCTGAGACCTGCCAGAACCTTGCTCTCAGCCCCAGT
AGCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAAGTAGGGCATTGC
TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCTTGGAATG

FIG. 4 (52 of 61)

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CTAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAAAT
ATTGGTCCTTGGGAACAGATTTTGGAGTCAAAGAGATGGACTTCAGATGG
CCAGATGCACTGCTTCTTTAGGGAATTCTGTGAAAGCTCCCTGCATTTAT
CTTAATACAGGCAGCAGATTTTCATGAGTACCCCCGAGGGATGGCCCCAGG
TCCTCCAGCCTGTGAGCATCCTTCTGTCTTCAGCAGCACCACAGTATCT
TTATATGTCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGAT
GTTCTGGCTGCCAAATTCTCTGTCAAGCGCCTCCAATTTTTTGTGTCTT
TGATTTACCCCCAATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGAT
ACTGCCAAACCACAAACAGGTTAAAATCAAATAGCAGATATCCCTGTTCC
TAAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCCTCCTTATTGT
TGAGTCCTGAAGCCCTTCTTGTCTATTTTTATTTTTTGCATGAACAATTT
AGTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTAC
ACAAACTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAAT
CACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTTGCT
CCACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAA
CTGAGATAGGGTGTGCAAGATTTATATATATAAATATATCTCTCCAACC
CCTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGG
GATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGT
TGCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT
CAGCAAACCTTCTATAGAAGGTGTGAGATGGTAAGTATTTTAGGCTTTGCT
TGCCAGATGATCTCTCACTAGTTAACCATGCTATTGTAGCCTCGAAGCA
GCCAGAGACAATATGTAAACAAGAGCATGGCTGTGTTCAATAAAACTTT
ATTTAAAAAACAGTCAGGGACCGGATTTGGCCAAAGGCCATAGTGTGCC
AGCCCCAAGACTAGAGCAATGCACTTTTAACTTTTTTATTTTTTGT
AAAATGCCAAGATCCACAAAAATGCTATTGCACCCCGTGTGTTAGCACTG
TGACTCAAGGTTTGGGAAATTCTGCTTTGAAGGCGTGATAGACAGGAGAG
CATGGTCTGGCCCCCTTGGTGCCTTTCTGGTTGCAGCGAGCATTTCAAAC
ACAGAGCAAGGCCAGTGGTCTGTTCACTAGAGACATGCAGCAAGGTG
TCCTGGGGTGAGAAGATGCCATAACTGGTCCCCCTTTCTATCTCCTTAGGT
CTTGGACTTCATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAAAT
GTCCTTTGTGGGGGAGAACTCAGGAGTGAAAATGGGCTCTGAGGACTGGG
AAAAAGATGAACCCAGTGCTGCTTAGAAGGTAAGGTTCTTGTAAGAAATC
TACCTCAGGGCCAAAGTGTAATTCCTAGAGCAGAACTTTGCTAGGTGCTG
TGCACAGACCCAGTTGTTTCTGCTGACTTGACAGTAAGTGAGCTTTCA
AATTTCCCTGGACAAATAACTAGACAAGAGAAATTCGGAAGAGAAAAGG
AAGCTTTGCTTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT
CCTCACCTACAGATTTGGGGCTTTAGCATCCTGTTTGCCAACTGGATGGT
TGCAATGCTTCAAATGCACCTCTTCCCTCCCAACATTTCCCAAGTGGA
GAGAAGCCTCCGATGAGAAGGAACTCTCTAAGGCTGGGCTGAACAAATGA
CCCAGGCACAGGGCATCTGAGTATTCATGAGGAACACATTTGGGTGTTG
CCCATGGGGGACAATAGGAGGAGGCTTTTGACCCAAATGATTGTCTACTG
AGGTGTGACGGGAGAGGCTGTGACATGCCAGAGGCCAAACCCGTGATCC
AGTTCATCTCTATTCTATGTTTCTGAAGAGGGAAAGCTATGATTTAATGTC
ATTACTATCATGCTGCTCTAGTATTTCTCAGCACATACAGAAAGAGGGA
ATTAAATGGTCCTTGATACCCCTAAATCCTTGGAAAATCCGAATTGCATA
TGCTAACCTCACTGCGTCTGACTGCAGACCCGGCTGTAAGCCCCCTGGAA
CCAGGCCCAAGCCTCCCCGCCATGAATTTTGTTCACACAAGTAAGGCCTC
GGGGTGAGGTGATGGGGGTGGCTGAGGTGCGAGGGTGGGGATGGGGGATG
GAGCCATTGGGTCTCTTACAGGGTGAGAGAATTGTAGAATGGGGACACC
TAAGGGTGCTGGATGGGGCTGAAGTCTTTCTTTGTGGAAGCAAATCCCA
TTAGGAGATAACTCTGGGAAAGATGAGCCCGGGGAGGGGCAGGTGATGCT
CACCTGCTAAGAGGCAAAGGGCAAGGAAGAGTTTGTGCTGGGAACCTTC
CAGGTGCTCTTCTGACCATAGCCAAAGAGACTGGAGACACAGACCTCCTC
CCAGCACTGAGGACAAACAGCCATGGGGCCAGTGGGGGTGCAGGGACACC
CACACCACTAAGGGCTCAGGGCGGCGCTTCAGAGCCTGAACCTTCTCT
CATGCTGCCATTTGAACACCACAACACCCTAATAGGAACTGTTAATATT
GCCACTTCTCAGGTGTGGAACCCGAGACAGACAGTGGAGATTCCCTGCCC
TAGGTGACACAGGTAATAAGTGACAGATGTGGAATTTAAAGGTACTATA
ACGTCTCTCTGCTGACTCAGGCTTAAGGCTCCCATCACCTCCTCTCTC
AGGACAGAGTCAGGAGGCCTCAGCCTGAGCCCCAGCTCTAGTGCAGGTTT

FIG. 4 (53 of 61)

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ATGTGGGAATACTGAGCCTACTAGTALCATGGCAGAGAGGACCAAATGG
GACCAGGTGTGTAAGGGTGCCTGGCACAGTTGGGGGAGGCTGCTGTGCT
TCTCCACCGCTGCTGCTGCAGTTACCTTTGATGTTTTAGTTTTGTTGTAG
TTACACCATTGCTGGCTTTGGATCTGCACTGTGTCCACTCCAGGTGGAAC
CACGCACACAAGCCTCTCTGTGCGGCCTGTCTGACTTCTCCTTGTGAGG
GCTGGGATCTCCTTCAAATCTGGCGGAAGTGGTTCTCCAAGTCTGGTCCT
CAAACGTGACGAGCATCAGCGCCTAGAAGTGTAGGAATACACATTCCCA
GGCCCCACCACAGACCTCCTGCCTCAGAACTCAGGGCGCTGAGGCTCTA
GGGGCTGCTTTAAACAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTC
TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCCTAAAGCTGGCGCTG
GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTCCCTATAGAAAACAA
CTGCCAGCACCTTAAGACCACTCACACCTTCAGAGTGGCCTTGAGAAAGA
TTTGGGGTCAAGGATCATGAGCGAGAACACCACTTAAGAGGATAGTGAAC
TAGTCTGCATGTGAGACGCTGAGATCCTATGTGAGGCTGTGATAGGAGGG
AAACAGAAACCAAAGGAAAGAACAGCTTTAAGAAGCGCTTAAGAGGTACA
AAGTAAAAATGATGGTGCTAGAAAAGTAGCTTCTTAAAAAGAGCATTTC
AGTCTCACCTGGACTAATGAATGAGAATCTCAGGAGTGTGAGGCCAG
GTATCCATGGTCTTAAATGCCACCCACCAGGTGATTCCCAGTGTGCACC
AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTTCAG
ACCAGCAGCACCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG
CACCACCCACACCTACTGAACCATAGTTTGCAGGTGATTTCTTGACATT
AAAGTGTGGGAAATGGAAAAGCTTAGAGTTGAGCTAGCTCGGTGACTCTC
AGTCAACCTGCACCTGCTCCATGAACTCAGACTGCCTGGGATGGGCCAG
AAAAGCTCCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT
CTCATCTGACCCCATATCACTGGGGAGTTACTTAGGATCTTGCTGGGGC
CAGTCATCTCTTCATAGACACTGAGAGTGTCCACGATGCTTGGGGCACT
ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC
CTGGGGAGCTTACAGTGCTATAGGGCAGCAAGCCAAGGATGCCAATACCT
GTGTGCAGGTACCCTGACGAGTGCAGAGCGCTGCAGCACCAGAGAGGAA
GCTACCCTGTGCAGAGGGGGCTGAGGAGGGCTGCAGGGAGATGACAGGAA
AGCCGGTGTACAGGAGGAGTCTCCCCACTCTTTGGGCATGAGGAGACC
AGGAGGACATTCTACAGTGAGAAACCCAGGCAGAGGCCATGTGCTTATGG
CATGGGAAAAGAATGACACCTTAGACTTATTCTCTACATTAGAAATGCCT
ACCACAGATACCCATATTATAGCTTCACATAGTGTGGTGGTTACTGTGTT
TTCATATTGTACATTTGCCATTTTCCAGCCACCCACCCATTCTTGACAG
TCACTGGCCCAGCCTGGGGGGCCCTGTTCTTTATCAAACAAGTGCTGAG
CTCTTTGACAGAGGTGAGGGTCACTGTCCAATCAGAGGCCAGGAGGGAAC
GTTCCCTTTTAAAGCCCTACTCTAGGCAGGCCTGGCCCAAATGAGTTGCT
AGGAGCCCACGCCCTAAGAACCCTCTGAGCACTGTTGTGGCTGGTCTGCT
TGCTAGAAGTTGTTCTCCAGGGCCAGGTGCAAGATTTGTGGCTTTTCAA
AGGAGCCCTAAAGCTCCAGCTCAGCCTTGACGGTGTGGGCTCCTGGG
GGCTTCTGCTCCCAACCTCCCACTCTTCCATCACCGCTCCCTTAGCC
TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCACTGCTGAGGGAATGATG
CCTCCAGTCAGAGGGTGCAAAAAAGAGAGTTAAGAAAAACAATGATTATA
AAAAGTCTTTTTTATACGCCAGACATTTCTTTGCTCAGGCTAAGTGCTA
CTTATTTGAGTAAGCATTTTAGTTCTCATAACTCCTCTCTCAAGTAGGTG
CTGCTATTACTTTTCAATTCACAGATGAGGACATTGAGGTTTGGAGAGACT
TAGTAACTTGTCTCTGCTCTACAGCAGAGCTGGGATTTGAATCTATCTG
TCCAAATCTGGAACCCATTTGCTTGACAGAAAGCTTAATTGCTTGTCCC
AGCAAGATAGAAAGCCTGGGAGTGGAAGAAATATTAGTGGCTGTGATGT
CTGAGCCACAGGCAGGGTGGAGAGCTAGGGCTGGGGCCCTTGACGTGG
GGAAGAAAGGGCTGAGTCTTCCATTTCAATGTGAAGTGTGATATCTGG
TGATATTGATCTAGGTCCAAAGGTGAAGAACTTAAACCCGAAGAAATCA
GCATTATGACCAGGATCAAAAGTACTGGTCTGGACTCTGGGAATCTC
ATAGCAGTTCCAGATAAAAACTACATACGCCCAGGTGACTCTCAGTTTTG
GCTGTGTTTTCTGCCTCCACCTAGCAGGGGTAAAGGCCTCCTGCTAGGTGG
GCTCAACTCCATGCTATACCATGCCCCATCTCCAGCAGGTGGTGGAGCG
AGGAGGAGAGGGCCCCAGGGACTAGGGCATCAGATGAAGGGTCTCTAGCAA
TGACCAGATCTGAAAGTAGTCTTTCTGGAAGGGCTGGAGAAAAAGAAGGA
GGCAGACACTTAGACTGGAAGAAGAGGAGGCTTAAACCGGTGTGATGGAG

FIG. 4 (54 of 61)

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GGAGAAGTGGACCACAGAGTCAAGGGAGAGGGACTGTGCATCAGGCCTGA
AACCCAGCAGACAGGAGAGACCTTCCCTGCTCTCAGAACCCACACATG
TTCTGACTGTCTTTTTCCAGAGATCTTCTTTGCATTAGCCTCATCCTTGA
GCTCAGCCTCTGCGGAGAAAGGAAGTCCGATTCTCCTGGGGGTCTCTAAA
GGGGAGTTTTGTCTCTACTGTGACAAGGATAAAGGACAAAGTCATCCATC
CCTTCAGCTGAAGGTGAGAGTTCTAGCTCAGTTTCTGGGCCTTTGGCTA
CQCCAAAGTAAAGGCCAAGATCCTCAATGCCCTCTCGCTTTCTGCAAAT
TCTTATCTTGGCCAATATAACAGGGACATCCACCTTTCTGGAAGCACCAG
GCAGAAGAGCCCCATAAATCTTCTCTGTTCTTGGCCCTTCTAGGGAA
GGAGGAGAGACTCCTCACAGCGGGGAGACAGCAAGGAGCTGAGCACCTGT
TCTCCTCTCCTGGGCTCACTGGTCTGCGCCCTGGGCGGTGGCGGTCCCC
TCCTGCTGTGGCCCTCCATGTGGCAAGCAACACAATTGGGCCAGGACCCT
GGCGTGCTGTGTAGGGTAGGAGGGTGTGAGGGAGCACTCGGAGGGCAGT
GTGTCTGCCCTGCAAATTTAGTCCTGGATGGAGCATCCTTTCACTTGAGG
GGAGAAATCTTAGGAAGCTGAATTAGATACAGATCTAAGCCATATTCTCT
AATTTTAAAACTATAGAGCTGAGATTTTGGTATCCATCTGACTCTTACG
TCTCTCTCTCTCTCTCTCTCTCTCAGTTTATTTTTAATCTGGGGACA
AGAAGGCCTGGAAGAGAGGGCATGATTGCTTATCATCCCTTAAATACCAG
TACCAAGGCTGACACGTCTCTTTCCCAAGGACCATCTGCCTTCTCTCTT
TTCCCTCCTCTCCTGTGTAAAGGCCTGGAGGATGAGCACATGTGCTGTGT
TTCCCTCCCTCTCAAAGCCTGTGCTATCTAATTAATCCCTTTTACCTCACA
GAAGGAGAACTGATGAAGCTGGCTGCCCAAAGGAATCAGCACGCCCGGC
CCTTCATCTTTTATAGGGCTCAGGTGGGCTCCTGGAACATGCTGGAGTCG
GCGGCTCACCCCGGATGGTTCATCTGCACCTCCTGCAATTGTAATGAGCC
TGTTGGGGTGACAGATAAATTTGAGAACAGGAAACACATTGAATTTTCAT
TTCAACCAGTTTGCAAAGCTGAAATGAGCCCCAGTGAGGTGAGCGATTAG
GAAACTGCCCCATTGAACGCCTTCTCGCTAATTTGAACTAATTGTATAA
AAACACCAAACCTGCTCACTAACTTTCTGTCAATTGGGTTCATTTCTCA
TTCATGCTTTAAGGATTTGTGTTTTTAGGATATAGCAAGAAGCTTGTTTA
ATTACAAAGTTCTGGGTTGGAAAGAGACCGGCTTCTGCTTGTGTACTGCT
ACCCTGAACCATCAGACATGCATGTGTGTGTCATATGCTATGATGTGGCC
AGTCTGAGTGCAATACTTGCAGCGGGAAGGAGCAGCTGGGTGCATGCTGT
GCTCTAGAATTAGTCTTTCTACTGGGGTTTGGTAGATTCTGAGGGCATT
GATCCTGGGGCAGAAGTGGCTGAGTCTGTGTCTAGGGTACAGTGTGCAAG
AAAGAAATGTAACAGCAAGTCAATCCAGCCAAGTGATAGTGGAAGAGG
GGTAGTTAGGTCCCAGATAAGGAGCAGGGTGACTTGACCTGTGGGAAAGG
CACAGAGACAAGGAATCTGGGTGAGTGACAGCCAGGAGACCAGGTGAGG
GAGGAGCCAGGTACTGTCTGGGAGGCTTGTCAACAAGGGCATGGTCTCTAT
CACTAAGCAGGGCTCAGATCCTCATAATGGGGGAGTGGAAGGCTGGCCGA
ACAGAAATCAGGGCCTGGAAACAGAGTGAGGGGGTGGAGACAGGAGACTG
AGGCTTGGAAATTAGTTTATTAGTTTTAGCTCTTCAGTTACAAGCAATAA
TAATAGCTTCTAGCTTATTTAAGCAACAAGTATACTACAAAAGGAGCTTT
CTAGAAGGATATTGGGTATATTCAATTTCTTACTGCTGTGTAACAAATTA
CCACCAACTTAGTGGTTTTAAACAATGCAATGTATTATCTTGCAATTATGG
AGGTGAGTCTGGAATGTGTCTCACTGGGCCAAAATCAAAGTATCAGCAGG
ATAGCATTGCTTTGGGAGGCTCTAGGGGAGAGTCAATTTCTTGCCCTTT
CCAGCTTCCAGAGGCCACCTGCATTCTTGCTAGTGGCCCACTCCCATC
TTCGCTGCTTGGGTTTTTCTCACACTGCTTTGCTCTGACCCTCCTGCCTT
CCTCTTTCACATATAAGAACGCTTGCAATTTACATCGGGCTCACGTCAAT
ATCCAGGATACTCTCCCGTCTCAAAGAGGCTTAATTTAATCACAGATGC
AAAGTCCCTTTTGCTATGTCTGTAAACATATACACAGGGTCTGGGGATTA
GAATGTGGACATTTTCGGGGTGCCATTATTCTGCCTATCATGTGAAGTAA
CTTTCAAAATGGAAAGACATGCTGAAGAAAAAGTCAGGGATTTCTGGCAG
GCCAGAAATGACAGAAGGCAGAAAACGTTGGTCCCATCACTCAGATGGGT
AAGAGCCAATCATGCTTTTTGTGAGTTAGCAAAAGATTGAGATTCGAAGC
AAAGCATGCAACTGCCCTAGTTTTGGGTGATGTGTGACTCCTTGGTCAGT
GAAGGGCAGCACACCTTGATCAATACTCCCTCCAAGACTGTATCCAACGA
GGCCAGTGATGTTCTCAAAGCAGAGCTAGAGAGCTAATCCAGGAGAGA
GGCGTGTGGGTGGTGGGCAGGAAGACAAAGCTCAGCCGTAAAGGAGTAGT
AGGGACAGCACCTTAGGCATGGAGGCTCAAGTGAGATGATACCCATGGGA

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AGGGCTGCAATGCATGALAGTTGGGGTTTTACCTCTCACCCAAAAGCCT
ACTCAATTTTTACTGCAAAAACATGTTATCATCATTATTTTTACTTAG
CCCACCTTCTCTGGCAATTTCCATAGGAAAATGCATTCTAAATTTCAA
CTAATCAGGGGACTTGGAGCCTCTGGACACCCCTTGTTCTTGCCACA
GTCCCTTGCAAGGTGCTTATCAGAGCGGCTCCATGCAGGGGCTCAGG
ACAGGATCAGATGTCAGTTGCACCAAGGGGCGAGGACAGATCCTCTCTG
CTEACCATGCAGAAGGGACTGTTCAGTGCACCGTCATGGTCTGTGATT
TCTGGTCCATAAGGGAATTTTCACATGCATCGGGTGATTGTCACATCAGC
ACAACACTGTGAGGAAGGCAGAGTGAGAAATTTGTGTGCCATTTTATAGG
TGAGAAAACAGATGCAGAGACATTAAGTAACTTCACCACAGTCATGCGGG
TTTTAAGTGGCAGACTTTAGGTGTTGTGACTCCTAGTCCAGAGTCTTT
GCACTGCCCCCTGAGGTGCTAAAACCTCTACTGTGCTTTAAGACTCACTTGG
GGAGCTTCTTAAAAAGAGAGATTGCACAACCTGAGATTCTTGTTTAACTG
TTTTGGGATGTAGCTCAGGGATCTAGCTGCCTTAAAAAAAACCTCCCA
AGTAATTTCTGATGCAAGCGGTTCTTTTTGTCCACCTTTGAAGAAACACT
GCCTCCTCCCCATACATTTTATTAGAAAATGGTAACATGTTTTCAGCCT
GAGAGCCATTTCTGGGTGACCGGACGTGCGCAGCCGCTGTACTAGCTTT
CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA
TGAGTCTGAACCATGGAAAATTCATTGTGTGGCACATCTGGTGGGTGT
GCACTGTCCCCAGCAGTGAGGCACCCAGTGAAGACAGCAGCTGGGAGAGG
CTTAGTTACATGCAGTGGGACAGTGTGGGCTAGACTGCTGAGCCCTCTGC
AGTTTACTCTGTGTGAGGCAATGAGGGTGAAAGGCTGATCAGACCCAGT
GCAGACCATACCCTCCAGGGAGACAGATATCAGTCAGGACAACCCCAAGT
GTAGCTGGAGAAGCAGTGCCAGGTATGACCGGATGTGTATCCAACAGG
AAATCTGCATATAAATATAAGAGGAGAAAATGAACAGATGTTGCTCTTAT
ATGTAGATATTTATGAAGAGCATATAATTTGTGTTTGTGTGTTTAAAGAA
GTTTATAAGTATGCCTTAAAAATGTATAGTATATACTGTAGGTATTTTT
CCATTAGATATTTTGTGTTTTCATACTTATCCACATTGACATTGTAGCAAC
AGTATAATATAACAACCTCCTCTACAAAAGCAGAAGGAAGTGAAGCTTTG
GAAGGAAGCACCCAGTGAGCTTGCCCTTTAGGTGGGTGCAGTGAGCAG
GAGTCAGTGAGGTGAGATCCTTTGAGAGGAGGCAATCATTAAACCAGGAA
ATCTGCATGCACTGCTGGCCACACCTAACCTTGGACAATGGTGTGTTGGA
GCGCCTTCCAGCTCTTAAGGCTTGCGATTTCTTTCTCTCACTCTTCAACC
ACGATGATTAAATCTTCTCTACAGAGTTGGACAATAAAGCCTTGAGTTC
CTGCCTCCCCCTGGTGTGATCACGAGGCATAGACATGGCCAGGAACATGTA
GGTGTCTTTGAAAGCTGAACAAGTTAGTAAATTTCAAACCTCATTTCACC
CACCAGTAAATGGGAATAATAATAAACCTATTTTACATAGGGTTGACAA
GAGGAGTAAAGAGGGATTCAATGAAAGTTCGTTATTATCATTGTAGTAG
CAGTGTGATAATATCAACTGAAAGTTCATTATCATTATTAGTAGCAGTA
TTGATAACCCCTCTTTCTGTGCCTTCTCACTGGTGGGCCCAGGCCATCAG
CAATGCCCAGGGTGTGATGGATCTCTGCTGCATCGGGCACCAGCTGTGTC
AATGGTGAGAACAGTACAAGGGTGGGCAGGGCAAGGCAGGAAGCAGCCAG
GAGCAGCAGCTTCATGGGGTGAAGATGTCAGGAGCTTAGGGACAGTCAGA
GCGGGTGTGCCTCCTCTTGTGGAGCCTTCTGCGTGGGTAGGAACTGCTG
CAGCTGTGGCCATGGATTACCTGAATATGGGTGGAATTAGGCATTCAGC
TGGGTTAGCTGTGCCTAGAAGGAGGAACTCTAACTGAGAACTGTCCCT
ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG
GTGTGCATGGGGATGGGTAAAGAGCCACACACAGGGCTGATGACTGAGTC
TATTTAGAACAATAGATGTAAATCTGATAATGTAAATGTGATAGATTA
TTTTGTCAATTAGAAATGGTACCATATAATTATATATACATAAACATG
TATACATATACACATATACATGTGTGTATAAACACACACAGTATTGTC
CCCTACTCATCCATAAACCTGATGCCCTTAGCTGGGATTCCAGCTTTC
ACTCTCCTCTCTGTCTGCTGTCTATATCCTCCCCATCCTGTAATTCT
GGCTTATATGCCACTTCTCCTAAAGCCCTCCCTCAATCCCTTGCTGGA
AGTGACATTTTCTCTTTGAGCTGCCCCCTGCTTGTGCTTTGGTGAGGTCA
GCTGTATTGCAGTACCTTGTATTGTGGTTGTACATCATCGTATAGAATT
AATTTCTGACACATTCCGTATTTTTCAAAGGGCCTAGTGTGGGGCTTTAA
CAGTAACTACGCCACCACGCCAGTTAATTTTTGTATTTTTGGTGAGGA
CAAGGTTTCAACATGTTGGCCGGGCTGGTTTCAAGCTCCTGACTTCAGGT
GATCTGTGCTCAGCCTCCTGGAGTGCTAGGATTGCAGGCATGAGCCA

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CTGCACCCAGCCACCTATCAAAAATTTAAGTGCCATTTTTATTTTTATT
TTTTGTAGAAATGGACAAGCTGATCGCAAAATTCACATGGAATTGCAGGA
GGTTCCAAATAGCCAAAAACAATCTTGAAAAAGAAGAACAAAGTTGGAGGA
TTTACACTTTCCAGTTTCAAGACTTAGCTCTTAGCTACAAAGCTACAGTA
ATCAGAACACTATGGTCCTGGCATAAGTGATGCTGGACAGGTGAGCCCCA
AAGTGGGACTTAACCTGTGAAGGTTCTTGGCCTTGCCCAGGAAGGAATTC
AAGGGCAAGCCAATGGGACAAGAAAACAGCTTTATTGAAGGGGCAGTATT
ACAGCTCCAGCCCTGTTACAGCTCCAGCCCTGTTACAACCTCTGACTACTC
CTGCACAGAAGGGCTACCCCTGTAGGCAGAGAGTAGCAACTCAGGGCAGTT
TTGCAGTCATTTATATCCACTTTTAACACATGCAGATTAAGGGACAATTT
ATGCAGAAATTTCTACGGAATTGGTAATAACTTTTGGGTCATGGAGTCAT
CATGGAAGGGGGCGGGAACTCCCTGGTGTGGCATGATGACGGTAAAC
TGATATGGCGAACTGGTGGGTATGTCACATGAAAAGCTCCTTCCACCCCA
GCCCTGTTTCAATTAGTCCTCGGTTTGGTCCAGTGTCCAAGTCTGCCTC
CAGAGTCAAGTCCCACCCCTACCTCTTAAGGAGAGATGTAAATACATGG
AATAGAATTGAGAGTCCAGAAATAATCTCATACATCTATGATCAATTGAT
TTTCAGCAAAGGTGCCAAGACCATTCAATGAGGGAAAGAATCATATTTTT
TTCAACAAATGGTGTCTGGATAACCACATGTGAAAGAATGCAACTGGGCCC
TTATCTCACACATAACAGAAATTAACCTCAAAATGGCTCAAACACTTAC
ATGTAAGAGCTAAAACATAATATTCTTAGAAGAAAACAGGGATATATCT
TTATGACCTTGGATTTGCTGGCTGATTCTTAAATGACACTGAAAGCACA
GCAACAAAAGAAAAAAAATAGGTAAATTGGACCTCATCAAAATTTAAAA
CTTTTATGCTGGGTGCACACCTGTAATCCAGCACTTTGGGAGGCTGAGG
CAGGAGGATCTCTTGAGCCCAAGAAGCTGAGGCTACAGTGAGCCGAAAT
GTGCCACTGCATCCAGCCTGGGTGACAGAGCAAGACCTGTCTCGAATA
AATAAATAAACAAATATATAATTATAGATCTCTGGATCTTGCCTTCGGAG
ACTGACTCAACTAACTGGTCTGGGTGGGAGCCCAGCCATTTGTATTTTT
GAAAACCTCTCAAATGATTTTACTGTGCAGCCAAGGTTGAGAATCACTGT
ATCATAGGGTTGGACTCCTAACTGGAAACAGTTTGCACCATCAGGTGTCTG
CAGCATTCTGATAATAGTTAAGCTTTCTCCTAGATTTTCTGATATTAGA
TGAGTCATGTTTACAAGTTTTTACCAAGAGACAAACTATCTTTCTGCCCT
TACTTTCTCTTATACTATTCTAATCCAGAACCTTTTGGAACTTCCAC
TGAGAGATGAATCTAGAAAAGTGACTCTCTTGGCTACAACAGAGAGTAATG
TTGGCCTGTTTGTGCCAGATCCAGTTGGTGCTGGTGGTGGGACAGCACCT
CCCTGAAATCCCCTCCTCTCCCGTCAGATTCAGTCCCCCATTTGCATCAC
GTACAATCATCACTATGGGTTTCTATTACCTTGCTAGGGCATTTGGAGGT
ACCATATATACCAACTATTAGTTTTGAGCCATGGTTCCCAAAGTGTGGAC
TGAGGGGCACCTCAGCACACTCAGAGGTGTCTGAGGATATTTAAATATT
CTGAAGAAAACACAGTGACATCTGTGAGGCCCCGTGAAAACCGTTGGCATT
AAATTGTCTCAACCCAATTGCTTAAGAAGCAGAACTGGCCAGGCACGGTG
GCTCACATCTGTAATCCAGCACTTTGGGAGGCCGAGGCCGGCAGATCAC
GAGGTCAGGAGTTGAGACCAGCCTGACCAACATAGTGAAACCCCGTCTC
TACTAAAAATATAAAAATTAGCCATGCATGGTGGCATGCACCTGTAACCC
CAGCTACTCAGGAGGCTGAGGCAGGAGAATTGCTTGAACCTGGGAAGCGG
AGGTTGTAGTGAGCCAAAATCGTGCCACTGCACTCCAGCTTGGGTGATAG
TGAGACTACATCTCAAAAAAAAAAAAAATGAGAGAGAGAGAGAAGCAGA
ACCATCAGGTGTTTCTTTTGGCTTAAAGTACTCTGTGAAGAAATTCCTGG
GACACGAAGGATACCATGAACTGAGAGATTTTGGGAACCTCTGCTTTAGA
AGCTGGAGGTAGCATTCTTGGGCACAGTACTGCCTTGGGATCAGCAAT
CCTTTTGTGGTGCATTTAGGTGTGGCAAGACAGCTCTTAGAGTGGGACC
GGGATGTGCTTGGAGACAGAGGGAAGTAGATTGAGCTGCCCCGATAAAGAC
ATGCCAGCCTGGCAGAGTGTAGTACTCATGTCTGTAATCCTAGTGCTTT
GGGAGGCTGAAGTGGGAGGATTGCTTGGAGCCAGGGGTTTGGATCAGCC
TGGGAAACAACAAGACCTCTACAAAAAAAAAAGAAAAAAAAAATTAACCA
CATGTGGTGGCATGCACCTGTAGTCCCAGCTACCTGGCAGGCTGAGGTAG
GAGGATCACTTGAGCCCAGGAAGGTAAGGATACATTGAGCCATGACTGTG
CCACTGCACTCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA
ATTAAATAAATAAATAAATATATAGTGGCCATGACATCCCTAGAAAGACA
AGGTCTTGGGAATAGGTAGAAGCCAAGGGAAATGAGAAATGAGAGGGGGC
CCTGGAGCTGGAACCTGGGGGAGCAGGATGGCCTCTGAGAAGTTCTTGATA

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GTGGTGTCACTGATGTGTCTGATGTTTAGTTGTAATTATTTGCTGGGCCC
CTGTCAATCCCTCATATCTGATAGCTCTTTGCTAGTCAAAGTGTGGTCTGG
GGATCAGCGGCATCAGCATCACTTGAGAACTTGTTAGAGATGCAGAATCT
AGAGCCCCACCCGGGACCCAGAAACAGAGCCTGCATTTTAACAAGCTCCC
CAGGTGATTCTCACACACACTCGCATTTGAGAAGCACTGGGCTAGTTGAC
AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTTGGCA
TTAGGATGTTTAAAAGTCCTCCAGGTGTTTCTAAAGCCAGGTTTGAGGAA
TTACTGGGCTGATACAAATGTTTTGTGATGATGCTTTGTGTGTGTGTG
TG
TGGTCACTTGGCACCAACACAGGAAACAATGGAAATATGTGAGCCATGA
CAGAAAGGTGAGGAGATAAAAGAAATTAGTGACATGAGAGGTACTCCTCA
GGTGTAGGAAAGAGGGTAGAGCAAACAGGTTTTCCACCATATGTTGGA
TAGGGGGTCAAGTAAATTTCTACTTAAAAATTACAAACAGGGGCTGGGCG
CGGTGGCTCATGCCTGTAATCCCGCACTTTGGGAGGCTGAGGAGGGCGGA
TCACAAGTCAAGAGATTGAGACCATCCTGGCCAACACGGTGAAACCGTG
TCTCCACTAAAAATACAAAAATTAGCTGGGCATGGTGGTGCCTTTA
TTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCTGGGAG
GTGGAGGTTGCAGTGGGCCGAGATCGCACCCTGCAATCCAGAGCGAGAC
TGTGTCAAAAAAAAAAAAAAAAAAGAAAATTCAAACAGGATGACCTAAG
CCTGCAGGACTTGGAGACATCTAGGTGACTGATACTCAGTCACAAAACAT
AATTGGTCACAGGCCTGATGAAATGCACAGCAGACCTTCAGATGGTATGC
ACTCAAGTGATATCCACAAGTCCACCTAAAGAAATGCTATATTCAGACAT
TTGGCATCAATCTCTATCAAACAAAGATAGTCAAAGCAATGGGTCCAA
AAACACTTTCTAAGACAAATTTCTATTTGCTTTTAATATCAGTCATCC
CAGCCCTTGGAAATAGAGGAGCAAATGATACCAGTGGTACCCTACCACAT
GCACCAAGGTATATATCTCTCATGCTCCATTTTCTCCCTCTGTCTACATC
ACTAATAACTCATTGATTTCTGGTGCAAGCCCTGCTGGGAGAAAAAGTCT
ACTCTGTACCTTGGAGCAAGTTGCTCAGAGTAGGTATCGAGGATAAAAT
TTGGAAAGTTAGAAAAGCTATTAGAAGGAGATCCTAGTAGTTGAAAACAC
AGCCTGGCCAAGTCAATGATGCTATTTCTCTCCCGCCTTGCATGTCC
ATAGCTAAGGAAGACAATTTAGGCTTGGGCTAGAGGATGGGAAAGGGCAA
AATTACTGATGCCACAGCCAGAGAGGTATTTAGTAATCTGAGGGTGAG
GACCACATACCTGGTTTCAAGGACGTACAGTGTGACAGCTGTGAGTGGAT
GCCTGGAGTTCTGGCGTGTCTTCTAGCACAAATGATACCTGAGACTCTTGC
ATCATTGGGAATAATAAAATGGAGTGGATAGATATGAAATTATGATGGC
AATAAGCAATCAGCTAATAGCTTCAATTGATGGGACAGATTAAAGATGGCT
GCAAATCCTTTGGTCCAGGTTTGGGATATAGGCAGCATTGTATTGGAAT
GCTGATAGTCTGAGGCCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA
ACAAGCCTCACTTTCTTCAATGTGTGTGACTGCTGTCTTGATTCCCTGGG
TGGCCAGTTCCATTTCGTGTGGTTCTTTGGTCCACTTGACTCTGGGGTGGC
TCTGTGATGGCTTGACCAATACAATGTAGTGGAAATGATGCTGTGCATCAT
TTCCAGCCTCTTCCAGCCTTAAGGAACTGGCACTTTTATTTCTGTCCCT
TGGAAATCTTGTCTTGCAACCCATCCATCATACTGAGAAATTCTAAG
CTGCCCCATTAAGAGGCCACATGGTGATAAATTGGGGCTTACATACAG
CCCTAGCTGTGCTCCTAGCTGACAAACAGTAGCAACTTGTCAACAGCGA
GTGAACCACTTAGGACTGTATACTCCAGCCCCAGTTGAGCAATGTGGAAC
AGAGTAAACCATCTCAGCTTAGCCCTGCCAAACTGCAGAAATTATGAGCA
AAATAATCCCTAGGCTTTGGGCTGATTGTTCAGATTACTGGAACAGA
ATTTGGTACCAGGGGTGAGGTGCTACAGCAATGAAAGCTTAAGACACGTG
ACTTTGGTTTTGGGTCTGAGTGGCAGGGAACTTGGCAGGCCTCAAGGAA
ACTTTTAGGGAGGGTTGAAGCATAGTGAGGAAAACAGTAGGGGAAGCTAG
AGGAAAAAATGATGCTTGGTATGTAGTGGTGGGAAGTTTAGCAAACTCG
CCTGATGTAATGTGGGAAATTGTAAGAACTCAGAACGATTTAAGGGCATG
TTTTATAGGTCCTTTAAGAACTTCTAGGCCAGGCGCAGTGGCTCATGTC
TGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGCGGATCACAAGGTGAGG
AGATCGAGACAATCCTGGCTAACATTGTGAAACCCCGTCTCTACTAAAC
TACAAAAAAATTAGCCGGCATGGTGGCGGGTGCCTGTAGTCCCAGCT
ACTAGGGAGGCTGAGGCAGAAGATGGCGTGAACCTGGGATGTGGATCTT
GAAGTGAGCCAGATTGTGCCACTGCACTCCAGCCTGGGCAACAGAGTGA
GACTCCGTCTCAAACCGAAAAAAGAAACTTCTAGGGC

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TGGTCCCGTGGAAGCCTCACACATGGTACACAAAGGCTGTCTTGAAAAGA
AACGTAAGTGTGTTTTTGGTTTAAATAAAATTGATTATAAATGGATAATG
CAAAACATTTTAAAGAATTTTACTAGCTTACATTAGCAGATTTGGATCCA
GTGATTGTTACATTCTGGTACTGAGCCCCTGAATTACTTCTTTGAGTAAG
GCATTATACCAAAGCTATTGATAGTTGGGCTTATAGGGTGATGTTTGAA
GAAGTACTAATGTCAAACCAATATTTACGGTTCGACAAGAGGACATCAG
AACTGGTAATCCTTATTACCATGACTGGCTGGACAGAATACTCAATGTAA
TGGGATTTCTTGCAAATAAAGACGGGGAAGATGTAAAAAGATGCCTGAA
CATTCAACATTAAATGAAAGATTTTCAAGAAGAAATATGTATACTAACTGCAG
CCTTATCAAGTATATGGAAAAACACAAAGTTAAACCAGATAGTAAAGCAT
TCCACTTGCTTCAGAAGTTTCTTACTATGGACCCAATAAAGTGAATTACC
TGAGAACGGGGTCCCTGTTTCTTGAAGACCCACTTCTACATCAGACGT
TTTCAACAGTTGTCAAATCCCTACCCAAAATGAGAATTTTAAACAGAAG
AAGAACCCTGATGACAAAGGAGCCAAAAAGAACCACCACCGGCAGCAGGGC
CATAACCACACGAATGGAAGTGGCCACCCAGGAATCAAGACAACGGTCAC
ACACAGGACCCCGCTTGAAGAAAGTGAGGCTTGTCTCTTACCCTAC
CTCAGGTGGACTTTTACGGCCTCAGACTATCCGCGTTCCAATCCACATG
CTGCCTATATCCCAACCCTGGACCAAGCACATCCCAGCCGAAGAGCAGTG
TAGGATACTCAGCTACCTCCAGCAGGCTCCACAGGACCCACGTGAGACA
CACGGGTACTGAGCTGCATCGGAATCTTGTCCGTGCACTGTTGTGAATGC
TGCAGGGCTGACTGTGCAGCTCTCCGTGGGAACCTGGTATGGGCCATGAG
AATGTACTGTACAACACACCTGCCAGTAGCCAAGTTCCTTCCACCGCT
TTTACAGATCGGGGTAGTGGCTTCCAGTTGTACCTATTTTGGAGTTAG
ACCTGAAAAGAAAGCGCTAGCACAGTTTGTGTTGTGGATTTGCTACTTTC
ATAGTTAACTTGACCTGGCTCAGACTGACCAGTACTTTTTTTTCCGTGAC
AGTCTATAGCAGTTGAAGCTGAGAATGTGCTAGGGGCAAGCGTTTGTCTT
CATATGTCATGAATTCCTCCAGTGTAAACAACATTATCTGACCAATAGTAC
ACACACAGACACAAGGTTTAACTGGTACTTGAAAACATACAGTAGGTGTT
AACTCAGTGAAATAACAGGACTCAAAGTAAGATTATTTTGGTACACCTT
TCTTTAGTGTCTTATCAGTGAGTTGATTCAATTTCTACATTAATCAGT
GTTTTCTGACCAAGAAATATTGCTTGGATTTTTCTGAAAGTACAAAAAGCC
ACATAGTTTTTTTCAAGAAAGGTTTCAAACCTCCTAAAGATTAATTTCCAA
GTATAAGTTTGTTTTTATTTTCAATCTATGACTTGACTGGTATTAAAGCT
GCTATTTGATAGTAATTAGATATATTCTCATTGATATAAACCTGTTTGGT
TCAGCAACAACTAAATGATTGTACAGACAATGCTTTATTTTTCTGT
TTGGTGTGTGCTGTGGGAAAAAGAAAGAGAGATCAGATTGTTACTGTGTC
TGTGTGAGAAAGAGTAGACATAGGAGACTCCATTTGTTCTGTACTAAGA
AAAATTCTTCTGCCCTGAGATGCTGTTAATCTATATAACCTTACCCCCAA
CCCTGTGCTCTCTGAAACATGTGCTGTGTCCACTCAGGGTTAAATGGATT
AAGGGCGGTGCAAGATGTGCTTTGTTAAACAGATGCTTGAAGGCAGCATG
CTCGTAAGAGTCATCACCCTCCCTAATCTCAAGTACCCAGGGACACAAA
CACTGCTGAAGGCCCGCAGGGACCTCTGCCTAGGAAAGCCAGGTATTGTCC
AAGGTTTCTCCCATGTGATAGTCTGAAATATGGCCTCGTGGGAGGGGAA
AGACCTGACCGTCCCCCAGCCCGACACCCGTAAAGGGTCTGTGCTGAGGA
GGATTAGTATACGAGGAAGGAACGCCTCTTTGCAGTTGAGACAAGAGGAA
GGCATCTGTCTTCTGCCCCCTCCCTGGGCAATGGAATGTCTCGGTATAAAA
CCCGATTTTATGTTCCATCTACTGAGATAGGGGAAAACCACTTAGGGCT
GGAGGTGGGACATGCGGCAGCAATACTGCTCTTTAAGACATTGAGATGTT
TATGTGTATGCATATCTAAAGCACAGCACTTAATCTTTACCTTGTCTAT
GTTGCAGAGACCTTTGTTTACGTGTTTATCTGCTGACCTTCTCTCCACTA
TTATCCTATGACCCTGCCACATCCCCCTCTCCGAGAAAACACCAAGAATG
ATCAATAAATACTAAGGGAACCTCAGAGGCCGGCGGGATCCTCCATATACT
GAACGCTTGTCCCTGGGCCCCCTTATTTCTTCTCTATACTTGGTCTCT
GTGTCTTTTTCTTTTCAAGTCTCTCGTTCCACCTAATGAGAAACACCCA
CAGGTGTAAAGGGGCAACCCACCCCTTCATTGCTGATTTGTGAGCGTGCT
TTAAGGTGAAAAAAGCATGAATGTAACTTCTTAAAAAGGTACAGCATC
CAATTCAAATATTTTGTCTGATTTTAAATGCTAGTTGATGTAGTGCTAT
TAAAATTTTGTTCACATGGACACAGAGAGGGGAACAACACATACCAGGG
CCTGTTGCGGGGTGGGGATGAGGGGAGGGAACTTAGAGGACAGGTGAACA
GGTGCAGCAGATCACCATGGCCACATATACCTATTTAACAACCTGCAC

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GTTCTGCACACGTATCCCATTTCTTTTTTTTTTAAGAAATAGAAAAAA
AATAAAATTTTGTTCACCTGATTCTTCCATTTTAAACTTGTTTGCATGTG
GTTTAGGATGCCCTTACTTCAGCAAAGGAGAAGGAATAGGAGGGCCTTAG
AATTTTTGAGGGAAAAAAACCCTATAACATACATTGTACTGTATCAAAC
ATTTTACATGAATGACACAAGTATTCTGAATAAAAAAATAATTGAACATT
GTTAAGAACAAGGTGTCATGTAATTTATTTTTCATAAATAAAAAATTAT
AGTGGCTTAGACTGAAAGGAACAGAGAATTTAAAAAATTAAAAAGAAGCC
TTAGTATATTTTGTATATAGTTTCCATGTGCCATATTGCCATAATTGG
ATGAGAATTTTTGACCTCTGGCAGGGTGACCCTATATTTTCANTNTATA
AAGCGTGCATCATACC

MVLKCHPTGDSQCAPGVRVTALGHATQRVSSIXQIIPQI.WECIRKTEAWIHPIILNIISI.QPGICPSI.SNKCI.SSI.QRSASA/
 EKGSPILL.GVSKDEFCL.YCDKDKQSQSIIPSI.QI.KEKI.MKI.AAQKESARRPFI.FYRAQVGSWNMI.ESAAIHGWIFCTSCNCF
 I:FPVGIXNXVDFDI.I.GKAQKRGTTUSE

FIG. 5

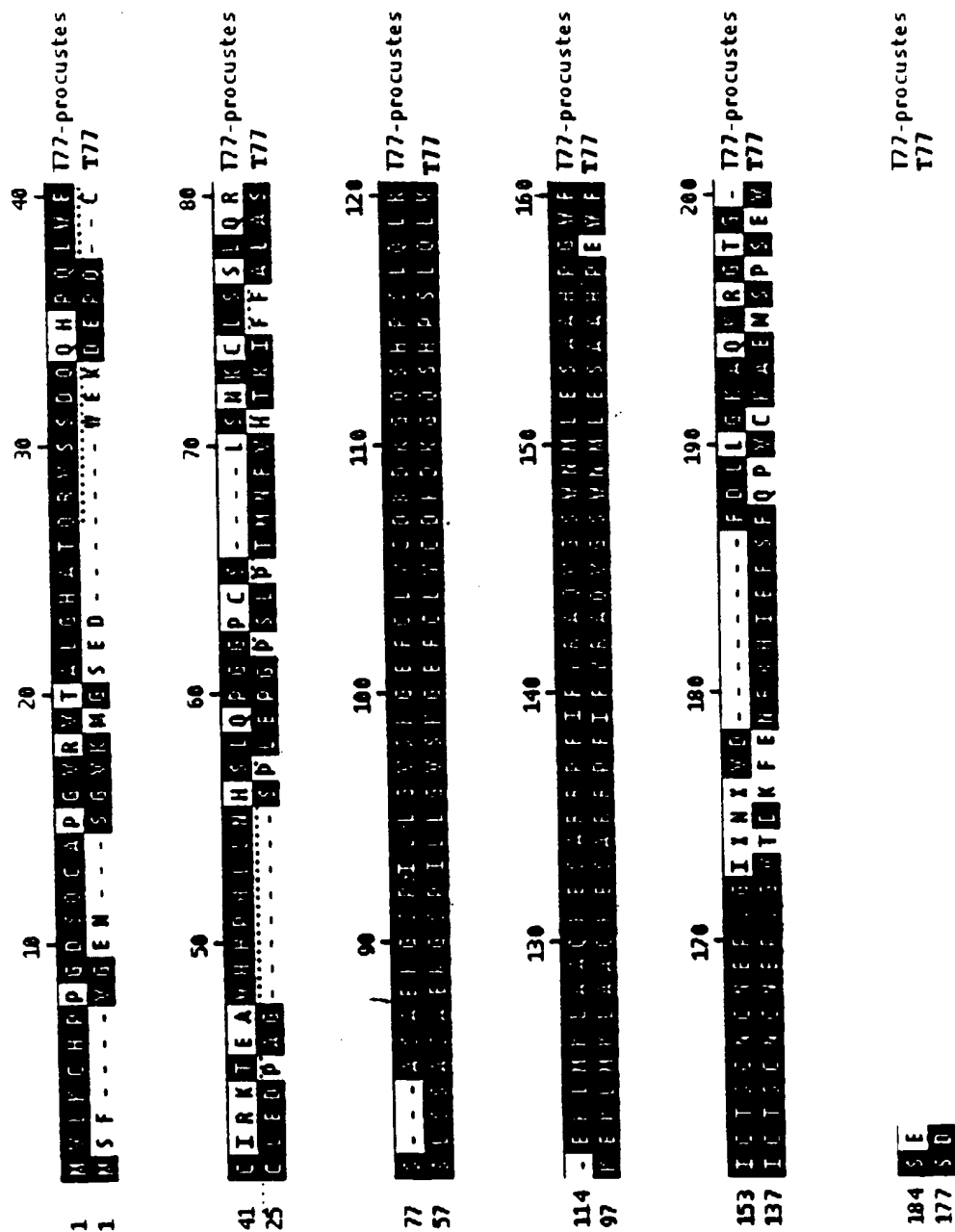


FIG. 6

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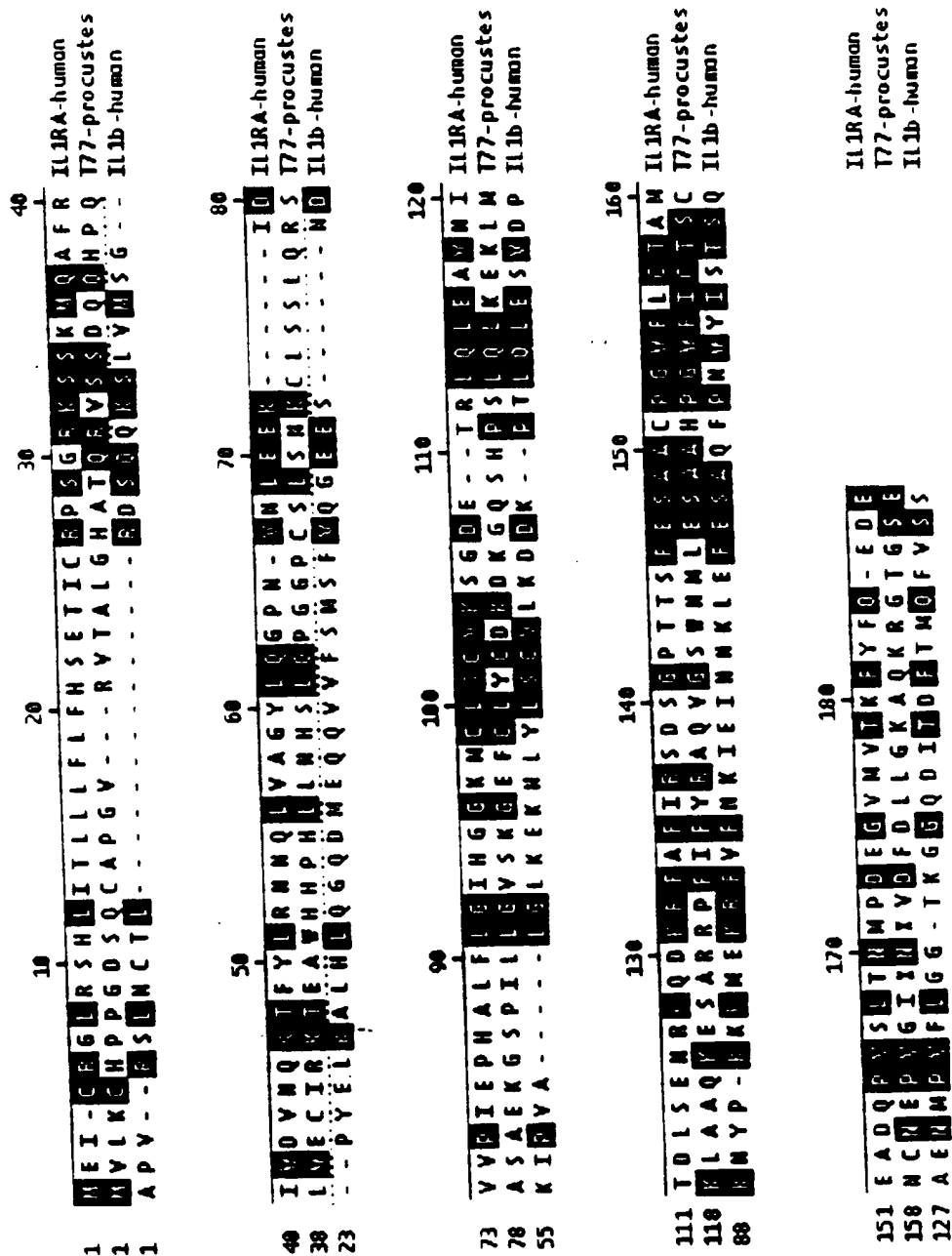


FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/16102

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53
US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* "A" document defining the general state of the art which is not considered to be of particular relevance	*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*B earlier document published on or after the international filing date	*X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*O document referring to an oral disclosure, use, exhibition or other means	*A document member of the same patent family
*P document published prior to the international filing date but later than the priority date claimed	

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